MAY 14, 1938

THE LANCET

Offices: 7, ADAM STREET, ADELPHI, W.C.2.

Telegrams: LANCET, RAND, LONDON. Telephone: TEMPLE BAR 7228 and 7229.

No. XX., OF VOL. I., 1938. LONDON, SATURDAY, MAY 14, 1938. Pp. 120—Price 1s.
No. 5985. VOL. CCXXXIV. Founded 1823. PUBLISHED WEEKLY. Registered as a Newspaper. Annual Subscription: Inland £2 2s. Abroad £2 10s.

OXFORD MEDICAL PUBLICATIONS.

SEE PAGE 2.

DISEASES OF THE THYROID GLAND
WITH SPECIAL REFERENCE TO THYROTOXICOSIS.
By CECIL A. JOLL, M.S., B.Sc., F.R.C.S. (Eng.).
Crown 4to. Fully illustrated. £3 3s. net.
Revista de Libros: "This book is the best clinical treatise which we possess to-day on the pathology of the thyroid. . . . The excellence of the text is generally enhanced by the illustrations."
William Heinemann (Medical Books) Ltd., 99, Great Russell-street, London, W.C.1.

3rd Ed., fully revised, 852 pp., 816 Illustrations.
EMERGENCY SURGERY. 50s. net; postage 8d.
By HAMILTON BAILEY, F.R.C.S.(Eng.).
Bristol: John Wright & Sons Ltd. London: Simpkin Marshall Ltd.

129 Illustrations (10 coloured). 12s. 6d. net; postage 6d.
DISEASES OF THE TESTICLE.
By HAMILTON BAILEY, F.R.C.S.
". . . one of the best monographs we have read."—*British Journal of Surgery.*
London: H. K. Lewis & Co. Ltd., 136 Gower-street, W.C.1.

NOW READY SECOND EDITION.
DISEASES OF THE RECTUM AND COLON
AND THEIR SURGICAL TREATMENT.
BY
J. P. LOCKHART-MUMMERY
F.R.C.S. ENG., M.A., M.B., B.C. CANTAB.,
Emeritus Surgeon to St. Mark's Hospital.
Pp. viii + 616, with 247 Illustrations. Price 35s.
Baillière, Tindall & Cox, 7 & 8, Henrietta-street, London, W.C.2.

PRINCIPLES OF MEDICAL STATISTICS
By A. BRADFORD HILL, D.Sc., Ph.D.
Pp. 172 + viii. 6s. net.
The Lancet Limited, 7, Adam-street, Adelphi, London, W.C.2.

Free to the Medical Profession on request. Clothbound Ed. 5s
ARTIFICIAL LIMBS.
"SOLVITUR AMBULANDO."
A Symposium on Prosthetic Achievement.
Pp. 72. 37 Coloured Plates.
"I congratulate you on this interesting, instructive and artistic production. I consider it to be a very great addition to my library."—M.B., Ch.B., F.R.C.S.
J. E. Hanger & Co. Ltd., 7, Roehampton House, Roehampton, S.W.15.

Works by ALEX. E. ROCHE, M.A., M.D., M.Ch., F.R.C.S.
UROLOGY IN GENERAL PRACTICE
3 Coloured Plates and 40 Figures. Demy 8vo.
17s. 6d. net; postage 6d. (*General Practice Series.*)
". . . a most attractive and readable book."—B. JNL. OF SURGERY.

PYELOGRAPHY
With an Introduction by SIR JOHN THOMSON-WALKER, F.R.C.S.
With 16 Plates. Demy 8vo. 9s. net; postage 6d.
". . . will be of great use . . . of interest and value."—B.M.JNL.
London: H. K. Lewis & Co. Ltd., 136 Gower-street, W.C.1.

MELANCHOLIA IN EVERYDAY PRACTICE.
By EDWIN HOPEWELL-ASH, M.D.
Includes chapters on manic-depressive psychosis; involutional melancholia; delusions and hallucinations; schizophrenia.
"We can recommend it."—GUY'S HOSPITAL GAZETTE.
John Bale, Sons, & Curnow, Ltd. Price 5s. 0d.

FRACTURES.
By MEURICE SINCLAIR, C.M.G., M.B., CH.B. (EDIN.).
With an Introduction by Sir ROBERT JONES, Bt., F.R.C.S
Pp. 550. 337 X ray photographs, photographs and diagrams. 24s. net.
Constable & Co., Ltd., London.

OESOPHAGEAL OBSTRUCTION:
ITS PATHOLOGY, DIAGNOSIS AND TREATMENT
(including four chapters on Cancer of the Œsophagus).
By A. LAWRENCE ABEL, M.S. Lond., F.R.C.S. Eng.,
Assistant Surgeon to the Cancer Hospital, &c.
Pp. 245. 132 Illustrations. 2 Col. Plates. 30s. net.
"Masterful and complete. . . Cannot be too highly praised."
—SURG. GYN. AND OBSTET. JOUR.
Oxford University Press, Amen House, London, E.C.4.

9 Plates and 135 Text Illustrations. 15s. net; postage 6d.
DISEASES OF THE
EAR, THROAT AND NOSE.
By J. DOUGLAS McLAGGAN, F.R.C.S. Eng. and Edin.
Surgeon in charge, Ear, Nose and Throat Department, Royal Free Hospital.
London: H. K. Lewis & Co. Ltd., 136 Gower-street, W.C.1.

Second Revised Edition. 82 Illustrations. 30s. net.
CANCER OF THE BREAST
AND ITS TREATMENT
By W. SAMPSON HANDLEY, M.S., F.R.C.S.
John Murray, Albemarle-street, W.

BY KENNETH M. WALKER, F.R.C.S.,
M.A., M.B., B.C.
THE ENLARGED PROSTATE.
New and Enlarged Edition. Pp. 223. Coloured Plate and 62 Illustrations. Price 14s. net. (Oxford University Press.)
SEX DIFFICULTIES IN THE MALE. (Second Edition.) 5s. net. (Jonathan Cape.)
PREPARATION FOR MARRIAGE. (Jonathan Cape.)

H. K. LEWIS & Co. LTD.

STITT, CLOUGH and CLOUGH'S
PRACTICAL BACTERIOLOGY, HÆMATOLOGY and ANIMAL PARASITOLOGY.
Ninth Edition. With 4 Plates and 208 other Illustrations. 8½ × 5½ ins. 30s. net; postage 7d. (*Just Published.*)

MACKENZIE'S ACTION OF MUSCLES:
Including Muscle Rest and Muscle Re-education.
By Sir COLIN MACKENZIE, M.D., F.R.C.S. Second Edition. With 100 Illustrations. Demy 8vo. 12s. 6d. net; postage 6d.

TUCKER'S INJURIES AND THEIR TREATMENT.
With 80 Illustrations. Demy 8vo. 9s. net; postage 6d.

SCHWARZ, GOLDBERGER and CROCKER'S
DIAGNOSIS AND NON-OPERATIVE TREATMENT OF THE DISEASES OF THE COLON AND RECTUM.
With 246 Illustrations and 9 Coloured Plates. Demy 8vo. 40s. net.

RAY'S RHEUMATISM IN GENERAL PRACTICE.
A Clinical Study. (*General Practice Series.*)
With a Foreword by Lord HORDER, *K.C.V.O.*
With 6 Plates. Demy 8vo. 16s. net; postage 6d.

SPENCER & CADE'S DISEASES OF THE TONGUE.
With 20 Coloured Plates and 123 Figures in the Text. Demy 8vo. 35s. net; postage 7d.

LONDON: H. K. LEWIS & Co. Ltd., 136 GOWER ST., W.C.1

BRONCHOSPASM AND ASTHMA

A booklet surveying this subject, which includes diagrams and illustrations, has recently been published and has been sent to all members of the Medical Profession. You are invited to send for a copy should this have failed to reach you.

"THE LANCET" writes (28/4/34, p. 929):—

"We have received a pamphlet on 'Bronchospasm and Asthma,' written to bring before the medical profession the value of Felsol in the treatment of asthmatic subjects. The powders can be prescribed by the medical man in accordance with the definite régime which he decides to adopt in the treatment of a case, the claim for felsol being that its administration relieves promptly the attack of asthma by its influence over bronchial spasm, so that only the most severe cases would require the injection of morphia."

BRITISH FELSOL COMPANY LTD.

Telephone: Clerkenwell 5862

Wigton House, 206/212, St. John Street, Clerkenwell, London, E.C.1

Telegrams: Felsol, Smith, London

Valentine's Meat-Juice

In **Hospital** and **Private Practice** and **in their own persons** when ill, **Physicians** have **demonstrated** the **power** of **Valentine's Meat-Juice** to **Sustain** and **Strengthen** the weakened **Vital Forces** when the **Digestive Organs** are **Impaired.**

Debility, Exhaustion and Anæmia

Ross H. Skillern, M.D., *Laryngologist, Rush Hospital for Consumption, Philadelphia, Pa.:* "I, myself, had the misfortune to be seized with an attack of Cerebro-spinal Meningitis and after a critical illness recovered. My mainstay during the attack was VALENTINE'S MEAT-JUICE, and I can assure it materially aided in my recovery."

For Sale by European and American Chemists and Druggists

VALENTINE'S MEAT-JUICE COMPANY

A-34 **RICHMOND, VIRGINIA, U.S.A.**

MAY 14, 1938

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, CHEMISTRY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 5985 LONDON: SATURDAY, MAY 14, 1938 CCXXXIV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ADDRESSES AND ORIGINAL ARTICLES

The Clinical Features of Central Pain. By GEORGE RIDDOCH, F.R.C.P. (*to be continued*) 1093

Histology of Diabetes Induced in Dogs by Injection of Anterior-pituitary Extracts. By K. C. RICHARDSON, M.Sc., and F. G. YOUNG, Ph.D. (*illus. plate*)..... 1098

Glomus Tumours. By A. W. KENDALL, F.R.C.S., and SYDNEY THOMSON, F.R.C.P. (*illus. on plate*) 1102

Subcutaneous Emphysema and Pneumothorax in Bronchial Asthma. By R. W. ELLIOTT, M.B. (*illus. on plate*)..... 1104

Radiographic Detection of Myelocele of the Unborn Fœtus. By J. F. BRAILSFORD, M.R.C.P. (*illus. on plate*)..... 1106

Cutaneous Application of Follicular Hormone. By Prof. B. ZONDEK, M.D. 1107

Vitamin A and Carotinoids in Blood: Deficiencies in Children Suffering from Xerophthalmia. By J. H. DE HAAS, M.D., and O. MEULEMANS 1110

MEDICAL SOCIETIES

Royal Society of Medicine: Section of Surgery: Non-malignant Stenosis of the Œsophagus 1112

A Mock Trial: Feather *v.* Watson at King's College Hospital 1113

REVIEWS AND NOTICES OF BOOKS

A Textbook of the Practice of Medicine. Edited by F. W. Price, F.R.C.P. 1114

Handbook of Practical Bacteriology. By Prof. T. J. Mackie, M.D., and J. E. McCartney, M.D. 1114

The Practice of Refraction. By Sir Stewart Duke-Elder, F.R.C.S... 1115

Treatment in General Practice. By Prof. H. Beckman, M.D..... 1115

Essentials of Psychiatry. By G. W. Henry..... 1115

Manual of Psychiatry and Mental Hygiene. By A. J. Rosanoff..... 1115

Principles and Practice of Clinical Psychiatry. By M. Braude, M.D..... 1115

LEADING ARTICLES

DOCTORS AND THE HERBERT ACT 1117

WAYS OF GIVING SEX HORMONES 1117

THE PREMATURE INFANT 1118

ANNOTATIONS

Salt as a Therapeutic Agent 1119

Prostigmin and Intestinal Motility..... 1119

Atelectasis after Anæsthesia 1120

Studies on Typhoid Fever on the Witwatersrand.. 1120

Testosterone in Graves's Disease 1121

Hospital Reports..... 1121

Experimental Peptic Ulcer 1122

Evacuation of Children from Threatened Towns 1122

Nursing Conditions in L.C.C. Hospitals 1123

Excluding Tubercle from the Services 1123

Bactericide within the Body 1124

Marriage Guidance Clinic 1124

NEW INVENTIONS

A Low-pressure Reducing Chamber for Anæsthesia. By J. E. ELAM, M.R.C.S. (*illus.*)..... 1116

SPECIAL ARTICLES

The Chemotherapy of Bacterial Infections. By Prof. L. P. GARROD, F.R.C.P. (*to be concluded*) 1125

United States of America: Broadcast on Rheumatism—New Food and Drug Law 1129

The Tavistock Clinic..... 1130

Opening of the New Westminster Medical School (*illus.*)..... 1131

Medicine and the Law: Lead Poisoning and Water-supply 1133

Infectious Disease in England and Wales.... 1130

Typhoid at Hawick..... 1130

THE LANCET 100 Years Ago 1143

GRAINS AND SCRUPLES

From "Silver Doctor" (II) 1132

CORRESPONDENCE

Blood Pressure in Scarlatinal Nephritis (Dr. J. D. Rolleston) 1134

Testosterone Propionate, the Anterior Pituitary, and Hyperthyroidism (Dr. A. A. Loeser)..... 1134

Pyloric Stenosis in Twins (Dr. D. Jennings)..... 1134

An Overcrowded Profession? (Dr. W. H. Hughes) 1135

Hearing-aids for Deafness (Mr. L. T. E. Webb)... 1135

OBITUARY

Arthur Pearson Luff, F.R.C.P. 1136

Lieut.-Colonel Edmund Wilkinson, F.R.C.S. ... 1136

Percy Furnivall, F.R.C.S. (*with portrait*)..... 1137

The late Dr. Grabham... 1137

Edward Gaved Stocker, M.R.C.S. 1138

Lieut.-Col. Herbert James Walton, I.M.S..... 1138

PANEL AND CONTRACT PRACTICE

Post-graduate Study—Lavish Prescribing 1138

PARLIAMENT

Notes on Current Topics: Local Authorities and the Blind—Better Rural Housing—Insanity and Marriage 1139

Question Time: Silicosis Certificates—Maternal Welfare—Prison Officers' Sick Leave—Diphtheria Deaths—Milk Schemes in Special Areas 1139

MEDICAL NEWS

Research in Tropical Medicine 1141

Plastic Surgery Congress. 1141

Physical Fitness in Prague 1141

University of London ... 1141

University of Birmingham 1141

Royal Medico-Psychological Association..... 1141

Kathleen Schlesinger Research Fellowship... 1141

St. Mark's Hospital, London 1141

Royal Statistical Society. 1142

West London Medico-Chirurgical Society ... 1142

Royal Medical Benevolent Fund 1142

Medical Tour to the U.S.S.R..... 1111

Education in the Open Air 1124

NOTES, COMMENTS, AND ABSTRACTS

Progress in Electro-encephalography 1144

Acute Non-suppurative Thyroiditis 1144

Thomas Stevenson 1145

Hearing-aids 1145

A Modified "Shipway" (*illus.*) 1145

A.R.P. in Factories..... 1146

Bad Taste..... 1146

The Interceptor 1146

Medical Diary 1142

Vacancies 1142

Births, Marriages, Deaths 1143

Appointments 1146

Well Illustrated ★ NEW BOOKS ★ Lucid Text

JUST PUBLISHED. 18 Illustrations. 10s. 6d.

THE SEASONAL PERIODICITY OF MALARIA

and the Mechanism of the Epidemic Wave

By **CLIFFORD A. GILL**, M.R.C.P., M.R.C.S., D.P.H., D.T.M. & H., Col. I.M.S. (Retd.),
Late Chief Malaria Medical Officer, Punjab.

A TEXTBOOK OF HEMATOLOGY
By WM. MAGNER, M.D., D.P.H. 29 Illustrations, including 3 Coloured Plates. 18s.

RECENT ADVANCES IN PATHOLOGY
By G. HADFIELD, M.D., F.R.C.P., and L. P. GARROD, M.D., F.R.C.P. *New (3rd) Edition.* 65 Illustrations. 15s.

REFRACTION OF THE EYE
Including Elementary Physiological Optics.
By C. GOULDEN, O.B.E., M.D., F.R.C.S. *New (2nd) Edition.* 181 Illustrations. 12s. 6d.

THE CHEMICAL ANALYSIS OF FOODS
By H. E. COX, Ph.D., D.Sc., F.I.C. *New (2nd) Edition.* 41 Illustrations. 21s.

J. & A. CHURCHILL Ltd., 104 Gloucester Place, **LONDON W.1**

OXFORD MEDICAL PUBLICATIONS

A New (Third) Edition of

A TEXT-BOOK OF MEDICINE FOR NURSES

By **E. NOBLE CHAMBERLAIN**, M.D., M.Sc., F.R.C.P.

Assistant Physician, Royal Infirmary, Liverpool; Physician, Birkenhead General Hospital; Visiting Physician, Smithdown Road Hospital; Lecturer in Medicine, University of Liverpool; Sometime Examiner in Medicine to the General Nursing Council for England and Wales, and Joint Nursing Council for Northern Ireland.

Pp. 478. 59 Illustrations. 8 Colour Plates. **20s.** net.

A new edition of our Medical Catalogue is now ready, and may be obtained on request from the address below. It contains particulars of more than 500 *books of medical interest, including* 100 *which have been published since the issue of our last catalogue. The following are examples of earlier titles which present features of value as reference works:—*

DISEASES OF INFANCY AND CHILDHOOD

Edited by **L. G. PARSONS**, M.D., F.R.C.P., and **S. G. BARLING**, C.M.G., M.S., F.R.C.S., with the assistance of 44 Contributors. In 2 Vols. Pp. 1834. 230 Illus. 71 Plates (6 in Colour). The Set **84s.** net.

GASTRIC AND DUODENAL ULCER

By **Sir ARTHUR HURST**, M.D., F.R.C.P., and **MATTHEW J. STEWART**, M.B., F.R.C.P. Pp. 561. 159 Illus. 10 Colour Plates. **63s.** net.

BONE GROWTH IN HEALTH AND DISEASE

By **H. A. HARRIS**, D.Sc., M.D. Pp. 263. 259 Illus. **34s.** net.

INDIVIDUALITY OF THE BLOOD IN BIOLOGY AND IN CLINICAL AND FORENSIC MEDICINE

By **LEONE LATTES**, translated by **L. W. HOWARD BERTIE**, B.M., B.Ch. Pp. 427. 71 Illus. **30s.** net.

INHERITED ABNORMALITIES OF THE SKIN AND ITS APPENDAGES

By **E. A. COCKAYNE**, M.D., F.R.C.P. Pp. 404. 2 Plates. **32s.** net.

AN ILLUSTRATED GUIDE TO THE SLIT-LAMP

By **T. HARRISON BUTLER**, D.M. Pp. 158. 5 Colour Plates. **30s.** net.

THE USE OF LIPIODOL IN DIAGNOSIS AND TREATMENT

By **J. A. SICARD** and **J. FORESTIER**. Pp. 244. 70 Illus. **16s.** net.

INJURIES AND SPORT

By **C. B. HEALD**, C.B.E., M.D. Pp. 567. 380 Illus. **25s.** net.

Oxford University Press

AMEN HOUSE WARWICK SQUARE LONDON, E.C.4.

ADDRESSES AND ORIGINAL ARTICLES

THE CLINICAL FEATURES OF CENTRAL PAIN *

By George Riddoch, M.D. Aberd., F.R.C.P. Lond.

PHYSICIAN TO THE LONDON HOSPITAL AND DIRECTOR OF THE NEUROLOGICAL DEPARTMENT; PHYSICIAN TO OUT-PATIENTS, NATIONAL HOSPITAL, QUEEN SQUARE, LONDON

No excuse need be offered for reopening the discussion on pain, provided that by doing so fresh light can be thrown on some of the problems it presents. For pain is a subject of perennial interest, as old as the study of medicine itself, and our understanding of the physiological and anatomical mechanisms which underlie it is still imperfect.

Pain is an affective experience, which among sensations, is, when evoked, prepotent; and is unique in that it is the only aspect of sensation which is accompanied by endocrine, autonomic, and motor reactions of a protective kind. Yet, because of its compelling and obtrusive characters, it is experienced only intermittently in the life of the healthy individual, its neural mechanisms lying dormant, but vigilant, ready to be awakened if the tissues of the body are threatened. The means by which it is kept under control has for long been one of the most discussed subjects in neurology, but without giving birth to a view that is generally acceptable.

Pain of central origin was chosen as the subject for these lectures because, whilst in recent years it has been absorbing the attention of neurologists in many countries, it is, except when of thalamic origin, less known in general medicine. It was therefore thought that a review of the clinical and pathological evidence, which has been steadily accumulating, and is recorded chiefly in neurological literature, might be of general interest.

By central pain is meant spontaneous pain, and painful over-reaction to objective stimulation, resulting from lesions confined to the substance of the central nervous system, including dysæsthesiæ of a disagreeable kind.

Central Pain with Thalamic Lesions

It is convenient to begin with pain from lesions of the optic thalamus since, of central pains, it is not only the most common but has been most fully studied.

Dejerine and Roussy [10] gave the first description of the thalamic syndrome which was later elaborated by Roussy in his "thèse de Paris." The chief features of the syndrome as described by them are as follows. On the side opposite to the lesion there are (1) acute, persistent, or paroxysmal pain, which is often intolerable, and is little affected by analgesics; (2) a variable reduction of cutaneous sensation, a greater loss of deep sensibility and some astereognosis; (3) slight hemiataxia; (4) slight transient hemiplegia, without contracture; and (5) choreic and athetoid movements. According to Roussy,[52] the pain and sensory loss alone are due to the thalamic lesion.

Head and Holmes [31] by the use of measured stimuli more fully analysed the sensory phenomena in thalamic disease, and came to the conclusion that the essential feature is a tendency to react excessively to unpleasant and, occasionally, to pleasant stimuli. This view has been amply confirmed by subsequent observers. So-called spontaneous pain occurs in a considerable proportion of such cases.

SPONTANEOUS PAIN

It varies from uncomfortable paræsthesiæ to pain of great intensity and diversity, but is often described as aching, shooting, or painful burning and may defy description. It is referred to deep or superficial tissues, is usually diffuse, and may be intermittent or persistent with paroxysmal exacerbations. It is notoriously intractable to treatment. The whole of the opposite side of the body may be the seat of pain or part of it may escape. Frequently the pain varies in position from time to time and it may change in character, for no apparent reason, during the course of the illness. As a rule it is aggravated by almost any form of somatic or visceral stimulation that can disturb consciousness, as well as by emotion, and is commonly associated with anxiety, which may be extreme. A state of apprehension of the same degree, as the result of pain of central origin, is met with only in some cases of concussion of the cervical spinal cord, in the acute stage, and is reminiscent of the dread of interference, which is familiar in patients suffering from severe causalgia or painful phantom limbs.

OVER-REACTION: HYPERALGESIA AND HYPERPATHIA

Whilst spontaneous pain may be absent in the thalamic syndrome, excessive reaction to objective stimulation of the affected parts of the body is, as Head and Holmes [31] insisted, the essential and constant feature. But in reality, as they believed, spontaneous pain is merely a further development of the same abnormality, for pain cannot occur without some form of stimulation. The characters of over-reaction are as follows.

Pain or discomfort is, in general, evoked by almost any stimulus which is capable of arousing a sensation. The threshold may be normal, increased, or diminished. Over-response without sensory loss is called hyperalgesia and, when associated with diminished sensibility to the form of stimulation which excites the painful reaction, hyperpathia.[20] But, whatever the threshold may be, the sensation evoked is abnormal. The painful sensation develops explosively. There is usually little relation between the strength of the stimulus and the amount of sensation excited; it is nearly "all or nothing." The pain is usually intensely disagreeable and unbearable and often evokes violent emotional and defensive motor reactions. It has a prolonged after-effect; that is to say, it persists for an unusual time after stimulation has ceased. Localisation of the pain is defective and irradiation over the whole half of the body is common. It might be added that, at all events when sensation is diminished, the pain is usually not simple but is complex and has frequently a thermal quality.

All stimuli are not equally capable of evoking pain and discomfort in thalamic syndromes. Those which are endowed with affective qualities are most potent and, in the presence of sensory loss, are, of somatic stimuli, alone effective. "The nearer a sensation approaches pure discomfort, the more certainly will the response be exaggerated on the affected side of the body." [31] But even in this category the potency varies, for deep pressure is more effective than pinpricks. Thus in Head and Holmes's series of

* The Lumleian lectures for 1938, delivered before the Royal College of Physicians of London on March 14th and 17th.

cases there was over-reponse to measured prick in 20 of 22, and of them the threshold was identical on the two sides of the body in 13, raised in 9, and lowered in none on the affected side. But deep pressure evoked excessive discomfort in all, the threshold being lowered in 15, especially in the hand and foot, was the same in 6, and raised in 3. In fact, pressure with the algometer was capable of evoking discomfort in cases in which there was complete analgesia to pinprick. Pressure with a blunt object is essentially different from pinprick in that it causes discomfort and crude diffuse pain rather than acute localised pain.[31] The increasing massiveness of the sensation it evokes with the greater threat it entails is undoubtedly a factor in its effectiveness.

With extremes of heat or cold, whether thermal sensibility is preserved or not, discomfort, if evoked, is greater on the affected side. The capacity to cause discomfort is greater with cold than with heat. Thus Head and Holmes [31] found that, in cases with a normal threshold, a warm stimulus was not described as hotter than on the normal side until the temperature was between 40° C. and 45° C. On the other hand, all but the mildest cold stimuli were said to be colder and more unpleasant.

The strength of the thermal stimulus necessary to elicit pain or discomfort depends upon the degree of sensory loss, but, even with complete thermo-anæsthesia, extremes of heat or cold (water about 50° C. or cold below 15° C. or melting ice) may evoke intensely disagreeable sensations, which, however, are devoid of any thermal quality.

In cases in which thermal sensibility is preserved, or only partially lost, the excessive response evoked is usually translated by the patient into terms of greater heat or cold whilst, on analysis, it is clear that it is only discomfort that is increased. Sometimes the sensation described is compound, as for example, in one of my cases in which hot water not only felt "hotter" but excited also a disagreeable bursting sensation under the skin. In this case, as in many others, the patient was especially intolerant to cold on the affected side. Cold water applied to his left side gave him a "shock, like electricity," and even a drop of rain on his left hand was sufficient to produce a violent reaction. In a case of Foerster's,[20] a drop of rain on the face caused violent pain like a wave of boiling water, and in another, burning pain was evoked, only on the affected side, on drinking cold water or passing urine.

Scraping and tickling are extremely uncomfortable and, if sensibility to light touch is unimpaired, even gentle moving contact, especially over hairy parts, may be intolerable. For example, one of my patients was so hypersensitive to touch that she could not bear to have anyone walk with her near her affected side. Even the contact of her clothes was disagreeable and dressing and undressing was a dreaded ordeal.

Stimuli which normally have no obvious affective quality may have its presence revealed in the thalamic syndrome. For example, the vibrations of a large tuning-fork which, on normal parts, appear to be neutral may give rise to discomfort, and movement of a limb may be very painful.

Like extremes of temperature and deep pressure, visceral stimulation is peculiarly efficacious in evoking excessive discomfort. Thus, testicular pressure is far more disagreeable on the affected side and may be capable of causing severe diffuse pain on the affected side even when there is gross analgesia. Referred pain from thoracic and abdominal visceral disease, in thalamic cases, also tends to irradiate widely. According to Foerster,[20] whereas pain on the normal side is more or less restricted to the dermatomes which correspond to the diseased organ, on the side affected by the thalamic lesion it is not only more severe but tends to spread over the whole half of the body.

The effect of persistent stimulation from active somatic lesions, such as a sore in the skin or a deep abscess, is illuminating and is well exemplified by one of Foerster's cases in which there was no spontaneous pain or hyperpathia until a few days after the patient burned his foot. Characteristic pain and over-reaction to stimulation over the whole side of the body then developed, and did not disappear until the burn had healed.

As a rule, somatic stimuli can cause or aggravate pain only when applied to the affected side. Sometimes, however, it is found that stimulation of the normal side may also give rise to exacerbations of pain (synæsthesalgia). Further, stimuli, to be effective, need not then be noxious, although such are most potent; for those which are neutral or even pleasant in the stimulated part may evoke pain on the affected side.[20] This phenomenon of synæsthesalgia led Foerster to conclude that both optic thalami are in close functional relationship.

As has been well known since the reaction was first described by Head and Holmes,[31] thalamic pain can be caused or aggravated, not only by somatic and visceral stimulation, but also by excitation of the organs of special sense. Thus a sudden bright light, a loud or unexpected noise, and less often an intense smell or strong taste,[20] particularly if unpleasant, may excite pain limited to the affected side of the body. Sad or distasteful music may cause a violent reaction as in Case 11 of Head and Holmes,[31] in which the patient had a horrid feeling on the affected side when the choir sang, and her leg, which was the seat of choreiform movements, screwed up and began to shake.

There has been much discussion on the mechanism by which these abnormal reactions from stimulation of the special senses are evoked—whether they are the result of direct action on the optic thalamus of impulses derived from the particular end-organ of special sense or not. According to Foerster, the optic thalamus is the meeting place for afferent impulses of every kind and from every source; in fact, it is the only situation in the central nervous system in which a general sensory convergence occurs. It is not therefore surprising that sensory impulses, whatever their origin, can evoke a similar reaction.

Ajuriaguerra [1] and Baudouin and Schaeffer,[4] nevertheless assert that since visual or auditory impulses do not possess affective qualities, they cannot by themselves evoke a painful over-response. According to these authors, the increase of pain on the abnormal half of the body excited, for example, by a loud noise, is the result of painful impulses derived from excessive stimulation of the ear-drum. They forget, however, that somatic stimuli which are normally neutral, such as light touch or passive movement, may sometimes produce severe pain.

But quite apart from the probable effectiveness by themselves of auditory impulses, the emotion they arouse, if the noise is disagreeable to the individual, must play a part in exciting the diseased thalamus to over-reaction; for it is notorious that anxiety and distress can be as potent, in this respect, as affective peripheral stimulation.

Head and Holmes [31] were also the first to point out that a general state of discomfort, ill-being, or

malaise and, less seldom, of pleasure or well-being, may be exaggerated on the affected side.

Over-response to painful and uncomfortable stimuli, with or without the presence of spontaneous pain, is admitted by all observers to be the characteristic feature of the thalamic syndrome. But over-response to pleasant stimuli may also occur, although only in a minority of cases. Head and Holmes [31] found that in several of their patients warmth (34° C.) was more pleasant on the affected than on the normal side. Further, in a few cases with thermo-anæsthesia, a warm object, when applied over a large surface, evoked pleasure but without a sensation of warmth. Foerster [20] has confirmed these observations and also found that gentle moving contact on the affected skin may be unusually pleasant.

Pain and discomfort are generally prepotent over pleasant sensations; but the possibility of pleasurable sensations, if massive enough, controlling pain was demonstrated in one of Foerster's patients. In this case spontaneous, violent burning pain on one side of his body was abolished and replaced by an agreeable sensation, when the patient was immersed in a lukewarm bath. Such examples must be exceedingly rare, but that they do occur is of great interest.

This case naturally leads to the consideration of clinical observations on the inhibition of thalamic pain. Whilst the usual response to painful or uncomfortable stimulation of the affected side is aggravation of the spontaneous pain, often over the whole half of the body, nevertheless there appear to be exceptions to this rule. Thus, Ehrenwald,[13] in one case, found that intense local excitation, as by firm pinching or faradisation, caused temporary disappearance of the spontaneous pain, except in the part directly stimulated, where it remained and with increased intensity. The same patient accidentally fractured his forearm on the affected side and, during the period of local pain from the fracture, the spontaneous pain was elsewhere inhibited. The same observer also discovered that the sensation of itching, produced by the application of an irritating powder, was sometimes associated with abolition of pain for so long as the sensation of itching lasted. These examples show that occasionally irradiation of pain can be controlled by local stimulation but at the expense of increased pain in the stimulated area.

Not only irradiation of pain but pain itself, if not severe, may be temporarily inhibited as the result of local stimulation. Thus, in a case of Foerster's,[20] scratching the anæsthetic skin evoked a disagreeable sensation which could be abolished by simultaneous light contact of the neighbouring normal skin. This interesting observation recalls the examples cited by Rivers and Head [51] of the control of pain and its irradiation in a recovering peripheral nerve area by simultaneous stimulation of contiguous normal and abnormal parts. The substitution of a pleasant sensation for pain by the application of warmth in Foerster's patient quoted above is another example of inhibition of one form of sensation by another and again brings to mind the experiment of Rivers and Head [51] in which the glans penis was gradually dipped into water at 45° C. A sensation of pain was first evoked but was replaced by one of cold, when a part containing cold spots was immersed. As soon as the water reached the corona, which is endowed also with heat, as well as with cold and pain spots, the sensation of cold was in turn suppressed and was replaced by a pleasant sensation of heat. As these observers concluded, such interaction between excitation and inhibition of impulses underlying different sensory qualities forms the basis of integration in sensation.

SENSORY LOSS WITH THALAMIC LESIONS

The only constant feature of the thalamic syndrome is over-response to stimulation with or without "spontaneous" pain. The involuntary movements, slight hemiparesis, and even the sensory loss included in the original description of Dejerine and Roussy [10] may be absent. Although Head and Holmes [31] found some sensory impairment (not necessarily to painful stimuli) in all their cases, varying from only a measurable change to severe loss, they insisted that the degree of over-reaction bore no relationship to the amount of loss of sensation. "But the existence of sensation of approximately normal acuteness opens the way for more impulses that can evoke an excessive response." [31]

Usually postural sensibility is more affected than cutaneous, but all forms may be diminished and many different sensory dissociations are found. Impairment of pain when present is always greater for pin-prick than for deep pressure. In some cases, there is no loss to pain, even with graded stimuli, but definite disturbance of other forms of sensation.[20] Sensibility to heat and cold may be unchanged, diminished, or abolished. With complete thermo-anæsthesia, discomfort may still be evoked by extremes of heat or cold, but the affective response is the same for both and does not possess thermal qualities. If, however, the sensory loss is not severe, there is no confusion between heat and cold, although discomfort is present.[31]

Irradiation of pain appears to be greatest when there is loss of the sense of localisation, but diffusion may become extensive without such loss, especially if spontaneous pain has been severe and continuous, and the patient's resistance to it is diminished.

Rarely no sensory loss can be detected in spite of the characteristic over-response (Lhermitte,[38] Baudouin,[4] Foerster.[20]) Thus I have had a patient under my care in whom, after a stroke, impairment of sensibility to pain, heat, and cold on his left side was for a time associated with hyperpathia. Sensibility to cold recovered before that to heat and, four days after his stroke, when his left hand was still insensitive to heat, cold—even from a drop of rain—evoked a violent reaction like an electric shock. Later, on the same day, sensibility to heat began to return and was also associated with hyperpathia. When, however, the patient's condition became stationary all sensory loss had disappeared but the over-response to thermal and painful stimulation persisted.

At the other extreme are cases in which anæsthesia, analgesia, and thermo-anæsthesia are so severe that only massive stimulation, as for example from strong pressure, water at 50° C. or below 15° C. in a large vessel, can evoke a response, which is then one of diffuse unilateral discomfort or pain. In such cases spontaneous pain may be as excessive as when sensory loss is slight. As has already been mentioned in a few cases of this kind recorded by Head and Holmes,[31] pleasure could also be evoked by the application of warmth over a large surface on the affected side but without a thermal sensation. Such examples reveal the elementary and non-specific character of affect.

THE DISTRIBUTION OF PAIN AND SENSORY LOSS

When there is diminished sensibility to pain, as there is in the majority of cases, the area of sensory

loss may cover the whole affected side of the body or be confined to part of it, usually upper limb and face or lower limb and abdomen. The same is true of spontaneous pain and over-reaction. According to Lhermitte,[28] pain is most often complained of in the upper limb, especially its distal part.

Foerster [20] has insisted that even when the analgesia is extensive it is not uniform, but is greatest in the distal parts of the limbs, diminishing towards the girdles, and in the lateral part of the trunk, diminishing towards the middle line. In the limbs, too, it is often most on the ulnar part of the hand and forearm and on the lateral or peroneal side of the leg and foot. In other cases the loss is global or circular, as in hysterical analgesia, but the upper borders are not sharp nor tend to be limited by joints or other prominent anatomical landmarks. Further, the skin round the mouth and eye, anus, perineum, and genitals is relatively less affected.

CERTAIN ANATOMICAL AND PATHOLOGICAL OBSERVATIONS, WHICH BEAR UPON THE OCCURRENCE AND DISTRIBUTION OF THALAMIC PAIN AND OVER-RESPONSE

Pain is not an inevitable consequence of lesions of the thalamus, for it is often absent, especially with tumours. In addition, characteristic spontaneous pain and over-reaction appear to be independent of the presence or absence of analgesia, short of complete abolition of all sensation on the affected side when, presumably, the sensory part of the thalamus is entirely destroyed.

Of the factors which play a part in determining whether pain will develop or not, only the situation and cause of the lesion will be considered at this stage.

As to the situation of the lesion, it is generally agreed (Dejerine and Roussy,[10] Head and Holmes,[31 32] Sager,[12] Foerster,[20] Ajuriaguerra,[1]) that for thalamic pain damage to the lateral nucleus is essential. It is in the dorsal part of this nucleus that cortico-thalamic, presumably inhibitory fibres terminate and, according to Poljak [46] they are derived mainly from the post-central cortex. Further, in those cases of thalamic pain and over-response without sensory loss which have been subjected to detailed histological examination the lesions have been confined to the lateral nucleus.[1] At the same time it must be admitted that occasionally damage limited to this nucleus has been found in cases in which pain was absent.[17] The lateral nucleus is supplied chiefly by the lenticulo-optic artery.[18]

According to Ajuriaguerra,[1] when pain is accompanied by sensory loss, the lesion also involves the ventral nucleus.

Judged by present pathological evidence, the median or internal nucleus and the smaller anterior nucleus do not appear to possess sensory functions.

In view of the experimental researches of O. Sager [12] and of Dusser de Barenne [11] in monkeys, clinicians have been interested in the possibility of representation of different parts of the opposite half of the body in the lateral nucleus. According to Sager's [12] work on the ape, in the sagittal direction the area for the upper limb corresponds to the whole lateral part of the nucleus, that for the upper limb to the middle and caudal regions, and that for the face especially to the caudal portions. Dusser de Barenne,[11 12] from his strychnine experiments, in general arrives at the same conclusions.

The limitation of pain, over-reaction, and sensory loss to a part of one-half of the body in a proportion of clinical cases suggests that there is also somatotopical representation in man, but satisfactory histological evidence is not yet available. Ajuriaguerra,[1] however, quotes three suggestive cases of pain limited to part of the body with pathological data.

In addition to the situation of the lesion the importance of the nature of its cause has been long recognised.

All are agreed that vascular lesions, especially softenings of the lateral nucleus, more often give rise to pain than lesions of other kinds. Lhermitte [29] has asserted that, as a rule, pain is apt to appear earlier with hæmorrhages than with vascular occlusions.

Tumours of the optic thalamus are notoriously painless in comparison to vascular lesions. Imber [36] found the thalamic syndrome to be rare in a series of 45 cases of thalamic tumour, and in a review of a number of reported cases of glioma, Ajuriaguerra [1] discovered that pain occurred only in 3. This must have been the striking experience of all neurologists and it raises the question of the importance not only of the comparative destructiveness of lesions of different kinds, but also of tissue reaction in relation to the development of pain.

Inflammations are also relatively painless, as well as traumatic lesions, although the thalamic syndrome from war wounds has been described by Guillain,[25] Faure-Beaulieu,[15] and Leri.[27]

Central Pain with Brain-stem Lesions

In the past sixty years many cases of pain of pontobulbar origin have been recorded. It must however be understood that pain and other disagreeable sensations are symptoms in only a small proportion of cases of central lesion in these situations. That it occurs in the brain-stem as often as it does is mainly due to the presence of the descending sensory nucleus of the fifth and perhaps also to some extent because at least a proportion of the fibres of the spinobulbothalamic tract appear to ascend at this level by series of short relays in the reticular grey substance.

The striking fact that no case of pain of mesencephalic origin has been reported may well be connected with the absence of sensory nuclei in this situation.

Bulbar are more common than pontine cases. Garcin,[23] who has made a special study of the literature of pontobulbar pain, discovered 56 examples of bulbar origin as against 28 of pontine origin, in all of which there were adequate clinical and pathological descriptions. In his analysis, the order of frequency of various lesions of the bulb were: (1) vascular, which constituted the majority, especially thrombosis of the posterior inferior cerebellar artery; (2) syringobulbia; (3) disseminated sclerosis; and (4) pontobulbar tumours. Of the 28 cases of pontine lesion, most (13) were of tumours, and it may be significant, from the point of view of tissue reaction, as a causal factor, that tuberculomas (8) were predominant.

The syndrome of thrombosis of the posterior inferior cerebellar artery, with which bulbar pain is most often associated, includes analgesia and thermo-anæsthesia in the trigeminal area, on the side of the lesion, and in the trunk and limbs on the opposite side, which are the result of damage respectively to the descending nucleus of the fifth and the crossed spinothalamic tract.

When pain or other disagreeable sensations occur within the analgesic areas, they tend to be referred more to the trigeminal region than to the opposite

side of the body and limbs. Thus in the case of a man of 57, pain in his right ear woke him in the night and spread to his eye, nose, lips, and the inside of his mouth with tingling of his tongue on the right side and in that order. The whole painful region throbbed with each heart beat but the pain diminished to an ache after he vomited. Pain was absent in his trunk and limbs.

Reference of pain to remote parts may, however, precede trigeminal pain as in the following case of occlusion of the left posterior inferior cerebellar artery.

The patient was wakened by a severe cramp-like pain in his left shoulder which spread down his arm. Soon afterwards pain developed in the trigeminal area first on the right and then on the left side and sensations of pins and needles and painful cramp appeared in his right upper limb and spread to his lower limb. The pain in his left upper limb and in the right side of his head and face soon disappeared, except for soreness of his right ear. It also diminished in his left trigeminal area but persisted in and round his left eye, as sensations of soreness and tightness. They were still present six months after the onset as well as sensations of aching and of painful cold in his right lower limb, particularly in the thigh, *which were aggravated by worry*. There were cutaneous analgesia and thermo-anæsthesia in the left trigeminal area, especially in the cheek, and in the right side of his body below the neck. Nevertheless, if the left side of his face were touched pain darted to his left eye. With his right hand warm water felt neutral, but cold water evoked a sensation of burning. Also pressure on his right lower limb increased the aching pain that was always present. Sensibility in the right side of his face and left side of his body appeared to be unimpaired.

This case presents points of considerable interest. First, pain began in the upper limb on the side of the lesion, for which the best explanation would seem to be involvement of spinothalamic fibres which were homolateral and uncrossed. Secondly, trigeminal pain first developed on the side opposite to the lesion and persisted as soreness in the right ear. Presumably the crossed quintothalamic fibres from the opposite nucleus were affected before the homolateral nucleus. Thirdly, the occurrence of hyperpathia in the left side of his face and in his right lower limb; and fourthly, the continuous pain in the right lower limb was aggravated by worry as is common in the thalamic syndrome.

Syringobulbia is occasionally associated with trigeminal pain, and Foix, Thévenard, and Nicolesco [19] have recorded a case of severe bilateral pain in the face in which, at autopsy, a small cavity was found in one descending root of the fifth and gliosis in the other.

Central pain from lesions of the pons has been discussed, amongst other writers, by Weisenburg and Stack.[64] It is a rare complication and whilst it has followed vascular lesions it appears to be most often due to tumours, especially tuberculomas. As an example, von Economo's case [62] may be briefly quoted.

A man of 35 complained of severe pain in his trunk and limbs on the right side, which kept him awake and for which morphia had to be given. On examination there was loss of sensation to pain and temperature in his right upper limb and half of his trunk and to heat in his right trigeminal area. Tactile and deep sensibility were unimpaired. The left motor and sensory fifth and the seventh were involved. Slight nystagmus, chiefly to the right, was present. Taste on the left side was unaffected. There was no paralysis of the limbs but the reflexes were perhaps brisker on the left than on the right side. At autopsy a tuberculous lesion was found, the largest part being in the pons at the level of the fifth sensory nucleus. It stretched from the upper part of the pons to the entrance of the left acoustic nerve. The left eighth nerve and the greater part of the vestibular tract of Deiter's nucleus were destroyed. The motor and sensory nuclei of the left fifth were damaged as well as the spinotectal and spinothalamic tracts and most of the lateral tegmental reticular substance. The median lemniscus had escaped.

The following cases, for which I am indebted to my colleague, J. Purdon Martin, are of considerable interest. In the first, the lesion was almost certainly due to a tumour, probably extramedullary. The salient features only will be given.

A woman of 54 was admitted to the National Hospital with a fourteen years' history of symptoms pointing to a right auditory nerve neurofibroma. Over a year before admission, and at a time when there was evidence of increasing involvement of the brain-stem, she began to complain of pain in the whole of the left side of her body from her head to her toes. She felt as if it were scalded and the burning sensation was aggravated by a hot bath. Her fingers were so painful that her nails could not be cut. But, in addition, every sensation in her left side had been unpleasant during the six months before her admission to hospital. On examination sensibility to pain was abolished on the right side in the distribution of the first and second divisions of the fifth and diminished in that of the third. On the other hand, over the whole of the left side from the face downwards, although sensibility of prick, heat, and cold was very defective, stimulation aroused sensations of an extremely disagreeable kind. All other forms of sensibility were intact on both sides of her body, except in the right trigeminal area. Because of the patient's critical condition operation was not advised. In this case, as in the last, pain and hyperpathia were associated with loss to pain, heat, and cold, all other forms of sensation being unaffected.

The chief points of interest in the second case are the restricted area of pain and hyperpathia and the absence of sensory loss.

A man of 59 was proved at autopsy to have suffered from telangiectasis of his brain-stem. During the course of his illness he complained of an aching pain which began in the little and middle fingers of his right hand and spread to the ulnar aspect of his right forearm. It was continuous, was apt to keep him awake, and was aggravated by various forms of stimulation, including movement of the affected parts. Careful examination, however, failed to reveal any sensory loss in his right upper limb.

GENERAL FEATURES OF PONTOBULBAR PAIN

The time of onset of pain, in relation to that of other symptoms, may be early or late. It can best be judged with vascular lesions and, in such cases, may coincide with the stroke, as is most usual, or may first appear several days or more after it.

Whether "spontaneous" or evoked by direct stimulation it has, in general, the same characters as pain of thalamic origin. It is perhaps less severe and is less associated with mental distress, but the difference is one of degree. The extent of irradiation of evoked pain again appears to depend, in part at least, upon whether or not the sense of localisation is affected. As in the case of the thalamus, pain and hyperpathia with pontobulbar lesions may be evoked by massive stimulation when sensory loss is gross and painful sensations are frequently compound, thermal

qualities, especially of burning, being common. As is often the case with hyperpathia from lesions at any of the appropriate levels of the central nervous system, any form of adequate stimulation may evoke a sensation of abnormal quality quite apart from the associated discomfort. These perverted sensations are common enough and are frequently described as thermal. Thus a sensation of disagreeable or painful burning may be excited by touch or pinprick.[41] Sometimes even gentle stimulation is unbearable, as in Spiller's case [54] in which a fly walking on the face caused very painful reactions.

Pain, although varying in severity, is usually continuous and subject to exacerbations either for no apparent cause or from objective stimulation of the affected parts. It may also, as in thalamic cases, be aggravated by emotional disturbance [54] (personal case, p. 1097), a sudden loud noise,[20 54] or strong visual stimulation,[20] but special sense impressions may, as in the thalamic syndrome, act, in part, through the emotions they excite.

The distribution of the pain is most often crossed, the face being affected on the side of the lesion and the trunk and limbs on the opposite side, because of the frequency with which the bulbar pain syndrome is the result of unilateral thrombosis of the posterior, inferior cerebellar artery. Occasionally in such cases trigeminal pain is bilateral, developing on the two sides either simultaneously [24 65] or successively [63] (personal case, p. 1097), and it is then due to involvement of both the descending root of the fifth and the quintothalamic fibres from the opposite nucleus which have crossed to the side of the lesion. Still more rarely, pain is confined to the opposite half of the face. As has already been mentioned, the pain is usually referred to the territory of the first and second divisions, but the third may not escape and then the tongue, gums, and inner side of the cheek may be involved.

With pontine lesions, pain in the face is most often on the side opposite to the lesion, as is, of course, the pain in the limbs and trunk.

Trigeminal pain is more common than remote pain and is usually more severe and persistent, but there are exceptions to this rule, for pain in the trunk and limbs on one side may form the chief complaint. It may be limited to part of the affected side, for example to the lower limb [41] (personal case, p. 1097) or to the forearm and hand (Martin's case, p. 1097). In a case of Foerster's,[20] micturition caused intolerable burning in the urethra on the affected side.

Some sensory loss to pain, to heat, and to cold is present, but not necessarily in equal degree, for the same dissociations may be found as with lesions at thalamic and spinal levels. Pain and hyperpathia may be present, as in some thalamic cases, even when analgesia and thermo-anæsthesia is apparently complete. Other forms of sensation may or may not be diminished.

Pontobulbar pains, whether facial or remote, are often but not invariably chronic. When severe, like most pains of central origin, they are comparatively resistant to analgesia remedies.

I have purposely excluded from consideration tic douloureux as a rare symptom of disseminated sclerosis because, in spite of some evidence to the contrary, its origin is almost certainly never mainly central. Clinically tic douloureux is a distinct syndrome clearly distinguishable from the trigeminal pains we have been considering.

(To be continued)

HISTOLOGY OF DIABETES INDUCED IN DOGS BY INJECTION OF ANTERIOR-PITUITARY EXTRACTS

By K. C. Richardson, M.Sc.

OF THE DEPARTMENT OF ANATOMY, UNIVERSITY COLLEGE, LONDON; AND

F. G. Young, Ph.D.

OF THE NATIONAL INSTITUTE FOR MEDICAL RESEARCH, LONDON, N.W.

(WITH ILLUSTRATIVE PLATE)

The work of Houssay and others has shown that the daily injection of suitable anterior-pituitary extracts into intact animals may induce the temporary appearance of the symptoms of diabetes mellitus. Young (1937) has further shown that if a large dose of a suitable extract is administered daily to dogs, the diabetic condition may continue after the daily injections cease, and apparently becomes permanent. Of 6 dogs treated with suitable extracts, only 1 failed to become permanently diabetic (Young 1938a). The permanent diabetes resulting from the injection of anterior-pituitary extracts differs from that following removal of the pancreas in that the pituitary animals are able to survive, apparently indefinitely, without insulin therapy, whereas depancreatised dogs will live without insulin for only a few weeks at the most.

In the present paper are recorded the results of the histological examination of the islets of Langerhans of 5 dogs which had received daily injections of a diabetogenic crude extract of ox anterior-pituitary gland. Pancreatic tissue was obtained from 2 of these dogs (Nos. 15 and 16) during the period of daily pituitary injections. Dog 15 was anæsthetised and the pancreas removed aseptically at a time when this animal had become resistant to the diabetogenic action of the injected extract; Dog 16 was killed when exhibiting a diabetic condition which was presumably only temporary. Tissues from two dogs which became permanently diabetic as the result of pituitary injections (Nos. 28 and 40) were also examined; their early history has already been given (Young 1937). Pancreatic tissue was obtained from the one dog which failed to become permanently diabetic as the result of suitable treatment (No. 41), one month after the last pituitary injection had been given. The early history of this dog has also been described already.

As organs of some of these dogs other than the pancreas were also examined a description of the results so obtained will be given.

METHODS

Zenker-formol (Helly), or a modification of this fluid described by Bailey (1937), were found to be the most suitable fixatives for the pancreas. With the exception of Dog 40, pieces of tissue were taken from the head, body, and tail of the pancreas in each case, the remainder of the organ being fixed in 10 per cent. formalin. A stain differentiating the alpha and beta cells of the islets of Langerhans, in a manner suitable for photomicrography, was devised by combining Heidenhain's iron hæmatoxylin with Mallory's phosphotungstic acid hæmatoxylin. Thin sections, cut in celloidin-paraffin, were mordanted in 3 per cent. iron-alum for 24 hours and overstained in Heidenhain's aqueous hæmatoxylin. After differentiation of the hæmatoxylin with iron-alum

until only a faint nuclear staining remained, the sections were transferred to phosphotungstic acid hæmatoxylin at 50° C. for one hour; then dehydrated and mounted in balsam. The Heidenhain azan modification of Mallory's triple stain was also used on celloidin-paraffin sections from this material (see Thomas, 1937).

The methyl-violet, congo-red, and iodine tests for amyloid were carried out on frozen sections of the material fixed in formalin. The sections of the pituitary gland, fixed in Zenker-formol, were stained by a modification of Mallory's triple stain using Altmann's aniline acid fuchsin and differentiated in saturated aqueous picric acid before staining with the usual aniline blue-orange G solution.

HISTOLOGY OF TISSUES OBTAINED DURING THE PERIOD OF PITUITARY INJECTIONS

DOG 16.—This animal was killed during the period of pituitary injections at a time when the diabetic condition was well established. His history is given in Fig. 4 of Young (1938b).

Pancreas.—Mitotic figures were present in the islets of this pancreas (see Fig III on Plate). In our experience the islet cells of a normal adult dog are rarely if ever seen in mitosis, and these findings in Dog 16 probably indicate an increased rate of proliferation in the islet tissue. In addition there is clear evidence of cellular degeneration in the islets of this pancreas. One or more of the beta cells in each islet were found to be greatly hypertrophied. The vacuolation of the cytoplasm and the varying degrees of pycnosis in the nuclei were typical changes in these cells. In some islets the degenerating cells had left large blank spaces in the islets. The alpha cells in all the islets examined were normal.

Pituitary gland.—The pars intermedia in this gland was apparently very active, the hypophyseal cleft being filled with colloid similar in staining reactions to that in the small vesicles within the pars intermedia itself. Small areas of proliferation occurred on the surface of the pars intermedia bordering the cleft. The chromophobe cells in these regions contained droplets of colloid similar to that in the cleft. The pars anterior and pars nervosa of the gland appeared to be normal.

DOG 15.—This animal received daily injections of pituitary extract for over six weeks. During this period the animal accommodated itself to successive increases in the dose injected daily by becoming resistant to the diabetogenic action of the extract after an initial response. His history is given in Fig. 3 of Young (1938b).

Pancreas.—Again in this pancreas the characteristic hypertrophy and degeneration of individual beta cells was noted. Mitoses were also found in some islets. In the islets of this animal more beta cells had undergone degenerative changes than in the islets of Dog 16 (see Fig. IV).

HISTOLOGY OF TISSUES OBTAINED AFTER INJECTIONS HAD BEEN DISCONTINUED

DOG 28.—The early history of this animal is given in Fig. 1 of Young (1937). He became permanently diabetic after 25 daily injections of crude anterior pituitary extract, and died 44 weeks after the beginning of the experiment. Death followed the cessation of insulin administration after a period of experimental insulin therapy. As has already been stressed (Young 1937), the administration of insulin was apparently not necessary for the continued well-being of this animal in its normal condition.

Pancreas.—In the material examined, which includes sections taken from the head, body, and tail of the pancreas, we have been unable to discover any islets of Langerhans containing normal alpha or beta cells. The islets have been replaced, in a remarkably specific manner, by a hyaline material giving similar staining reactions to those of collagen (see Fig. I). The tests for amyloid in these hyaline areas were negative. The hyaline degeneration was so far advanced in the majority of the islets that not even degenerated cells resembling alpha or beta cells could be distinguished. The boundaries of the atrophied islets were seldom as clearly defined as in a normal pancreas, since the hyaline material often extended between the adjacent acini and covered a greater area than is normally occupied by a single islet. Fragments of degenerated acini were commonly found within the hyalinised areas.

The acinar tissue showed a condition of subacute pancreatitis in all the material we have examined. This confirmed the original macroscopical findings (Young 1937). In some lobules there were small areas of necrosis and hæmorrhage, with inflammation of the interlobular connective tissue. Apart from these localised lesions, the alterations in the acinar tissue appeared to be associated with obstruction of the duct system and with fatty infiltration of the duct epithelium. There was no extensive degeneration of the acinar epithelium and stages of zymogenesis could be detected in most of the sections.

Pituitary gland.—The sinusoids of the anterior lobe were extremely congested but there was no conspicuous degeneration in the glandular tissue which contained normal alpha, beta, and chromophobe cells. In comparison with the other dogs there was an unusual number of vesicles containing colloid in the pars intermedia.

Adrenal glands.—Apart from small areas of lymphocytic infiltration in the cortex, these glands appeared normal.

The *thyroid gland* was of the inactive type, having follicles distended with colloid and lined by a flattened epithelium. The gland was not obviously enlarged.

DOG 40.—This dog, which is still alive, became permanently diabetic at the end of May, 1937, following 16 daily injections of anterior pituitary extract (see Fig. 3 of Young 1937). He excretes about 100 g. of sugar daily on a moderate protein diet. He first received insulin, 50–60 units per day, at the beginning of January, 1938, when the tail of the pancreas was removed for examination at a biopsy operation.

Pancreas.—The islets of Langerhans were intact in this piece of pancreas. Some islets were quite normal but the majority showed cytological changes which were apparent only in the sections stained specifically for the various cell-types. No evidence of extensive degeneration could be detected in the beta cells. In almost all the islets, however, groups of beta cells lacked specific cytoplasmic granules, although the cells were not hypertrophied and their nuclei were normal (see Fig. II). We regard the loss of the specifically staining granules in the cytoplasm of the beta cells as indicative of functional exhaustion. The remainder of the beta cells and the alpha cells in most islets showed sharply staining cytoplasmic granules densely crowded in each cell, as in the normal pancreas. By comparing the reticular fibre pattern in silver impregnated sections of the pancreas from this dog and from Dog 41 (see below), it was evident that a slight degree of fibrosis existed in the islets of Dog 40. The islets were commonly found to be subdivided by the reticular fibres into groups of normal and agranular beta cells. In a few islets hypertrophy of individual beta cells was noted. The latter phenomenon was much less conspicuous than in the cases of Dogs 15 and 16. No abnormality was found in the acinar tissue and its duct systems beyond a slight degree of fatty infiltration of the duct epithelium.

HISTOLOGY OF TISSUES OBTAINED FROM A DOG WHICH DID NOT BECOME PERMANENTLY DIABETIC AFTER PITUITARY INJECTIONS

Dog 41.—This dog, the only one in six, failed to become permanently diabetic, although a severe temporary diabetic condition was produced. The animal was killed one month after the last injection of extract.

The pancreas, adrenals, thyroid, and pituitary gland of this dog were normal. The islets of Langerhans in this dog appear to provide a normal control for comparison with the islets in the rest of the series. No stages of functional exhaustion, hypertrophy, or degeneration in the beta cells have been found. The reticular fibres, in contrast with the condition described above in Dog 40, were confined to small networks accompanying the capillaries and forming a thin capsule around the periphery of each islet.

DISCUSSION

Richardson and Young (1937) found that the daily injection of a crude anterior-pituitary extract into rats resulted in a substantial hyperplasia of the islet tissue. In the present paper the pancreatic islet tissue of the dogs killed during the period of pituitary injections (Nos. 15 and 16) showed unusual mitotic activity. It seems possible that one response of the dog's pancreas to diabetogenic pituitary extracts is hyperplasia of the islet tissue. A functional proliferation thus induced might account for the ability of the dog to become resistant to the diabetogenic action of a given daily dose of extract (cf. Young 1937, 1938b). As well as mitotic figures, the pancreatic islets of Dogs 15 and 16 contained some hypertrophied and degenerating cells. These are similar to those described by Weichselbaum (1911) in the diabetic human pancreas, and by Allen (1922) as occurring in the pancreatic remnants of his dogs made diabetic by suitable dietary measures following partial pancreatectomy. The onset of diabetes in Allen's animals was accompanied by functional exhaustion of the beta cells in the small amount of islet tissue remaining. Following the loss of cytoplasmic granules, the beta cells hypertrophied and the majority became vacuolated and disappeared after degeneration of the nuclei. The term hydropic degeneration has been used to describe this process.

In a long series of experiments Allen showed that the severity of the diabetes could be correlated with the amount of hydropic degeneration in the beta cells. When the islets in his material contained only a few hypertrophied and vacuolated beta cells, the diabetic symptoms were very slight. The removal of a further fraction of pancreas with a suitable change in diet increased simultaneously the diabetic symptoms and the amount of degeneration in the islets. In these cases of severe experimental diabetes Allen obtained hydropic degeneration in all the beta cells. This extensive degeneration was followed, in most instances, by general atrophy of the islet tissue.

As is well known, hydropic degeneration has been found only very rarely in human diabetes. In Allen's opinion (loc. cit.) this is due either to its being missed in mild cases or to the probability that post-mortem changes make it difficult to identify. We believe the present experiments have an important bearing on this problem. In Dog 40, permanent diabetes is associated with hydropic degeneration in only very few individual beta cells of the islets we have examined. This type of degeneration cannot be regarded as a prominent lesion in the pancreas of this permanently diabetic dog. The fact that the material was taken at biopsy excludes the possibility that these findings were influenced by post-mortem changes. This therefore seems to constitute a clear-cut case of experimental diabetes, in which there appeared to be no extensive hydropic degeneration in the islet tissue. Warren (1930) states that in his experience hydropic degeneration in human diabetes is very rare, but may occasionally be found in fulminating cases of relatively short duration. It seems likely that hydropic degeneration occurs as the result of a rapidly developed and excessive strain on the islet cells. The removal of a large fraction of the pancreas combined with dietary measures, or the injection of a diabetogenic anterior-pituitary extract (cf. Dogs 15 and 16) may provide such a strain. The strain imposed on the islet cells need not be associated only with a diabetic condition.

DESCRIPTIONS OF ILLUSTRATIONS ON PLATE

MR. RICHARDSON AND DR. YOUNG

FIG. I, Dog 28.—(A) Portion of a lobule of the pancreas (× 40) showing hyaline replacement of the islets of Langerhans (H). (B) A hyalinised islet (H) in which only fragments of acinar and duct epithelium can be identified. The islet tissue has atrophied completely. (× 240.)

FIG. II, Dog 40.—Normal alpha (A) and beta (B) cells, surrounded by beta cells (X) which are devoid of cytoplasmic granules and presumably in a state of functional exhaustion. This is typical of the majority of the islets of Langerhans in the piece of pancreas taken at biopsy. N.B.—To give sufficient contrast between the granular and agranular beta cells for reproduction, the photomicrograph has been taken from an over-stained preparation. (× 680.)

FIG. III, Dog 16.—Showing an unusual number of mitoses (M) in two islets of Langerhans. X=degenerating, hypertrophied islet cells. The section was not stained specifically to show the cell types. (× 470.)

FIG. IV, Dog 15.—Hydropic degeneration in individual islet cells (X). The section is not stained to show the cell types. (× 370.)

We have found that a sublethal dose of colchicine given to normal rats causes, within eight hours, excessive hypertrophy and vacuolation of the dividing pancreatic islet cells without affecting the blood-sugar level. The hypertrophy and vacuolation stages in hydropic degeneration cannot be regarded, therefore, as specific changes associated with diabetes alone.

It has been claimed, particularly by Warren (1930), that many cases of human diabetes show no cytological changes at all in the islets of Langerhans. The islets appear to be normal even in respect of the granule content of the beta cells. In Dog 40 there are a few normal islets but the majority so far examined show stages of functional exhaustion of the beta cells. Many of the beta cells lack cytoplasmic granules, although otherwise they appear to be healthy cells. They have normal nuclei and show no signs of degenerative changes in the cytoplasm. It should be emphasised that all the islets of Dog 40 would have appeared normal if special fixation and staining had not been used to demonstrate the presence or absence of beta cell granules. We have not found all the beta cells to be normal in any dog in the present series except No. 41, which failed to become permanently diabetic following treatment effective in 5 other dogs, and which was killed one month after the last injection. During this period traces of

MR. RICHARDSON AND DR. YOUNG : HISTOLOGY OF DIABETES INDUCED IN DOGS BY INJECTION OF ANTERIOR-PITUITARY EXTRACTS

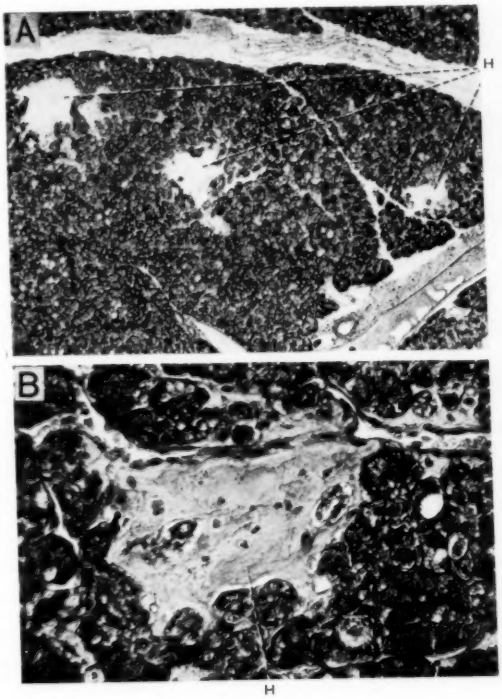


Fig. I

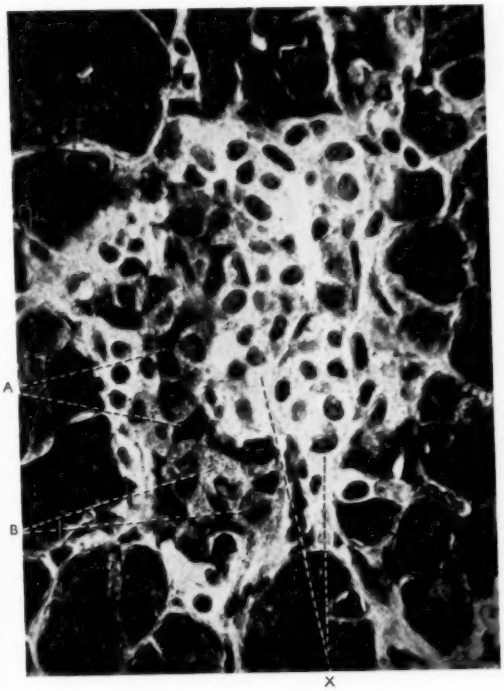


Fig. II

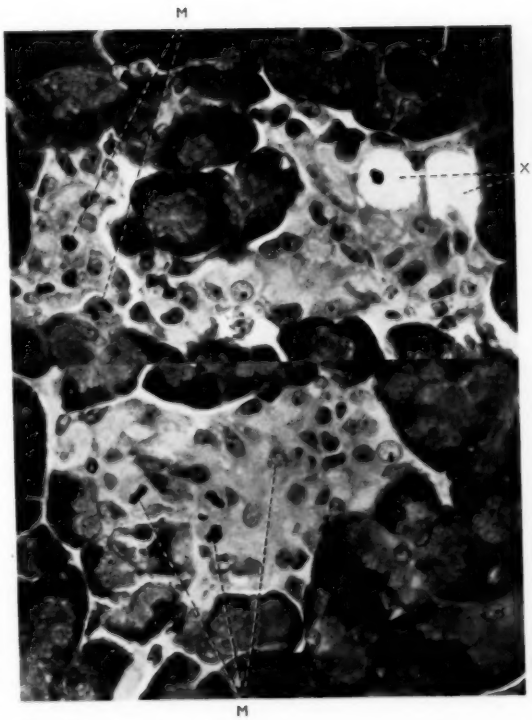


Fig. III

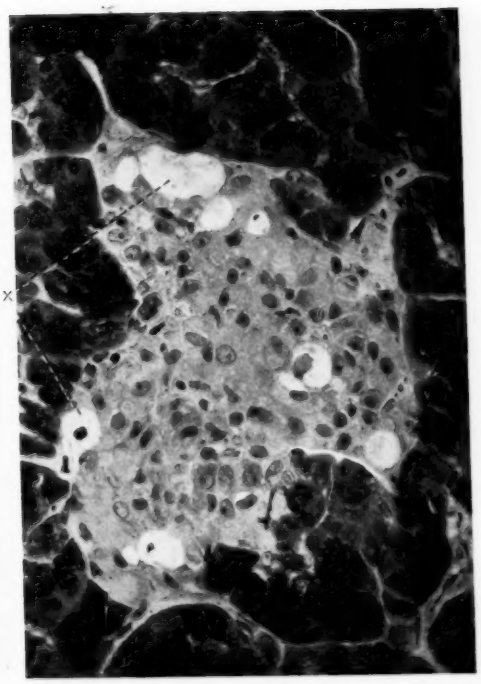


Fig. IV

MR. KENDALL AND DR. THOMSON: GLOMUS TUMOURS

Fig. I

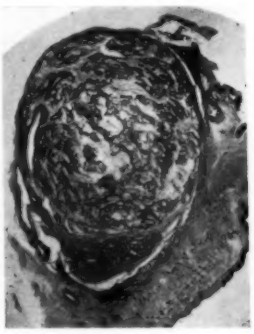


Fig. II

Fig. III

Fig. IV

DR. ELLIOTT: SUBCUTANEOUS EMPHYSEMA AND PNEUMOTHORAX IN ASTHMA

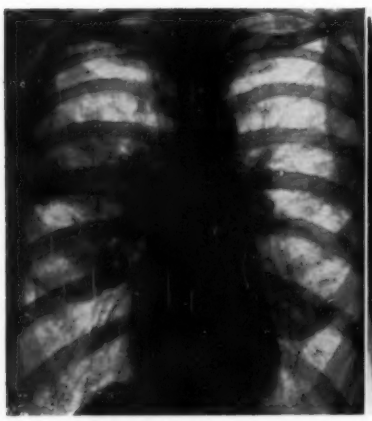


Fig. I

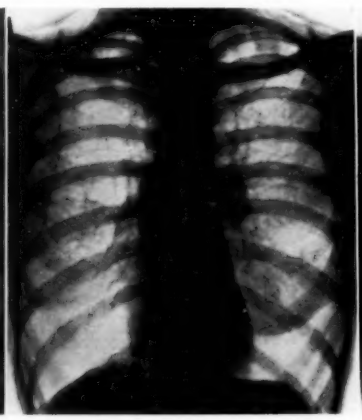


Fig. II

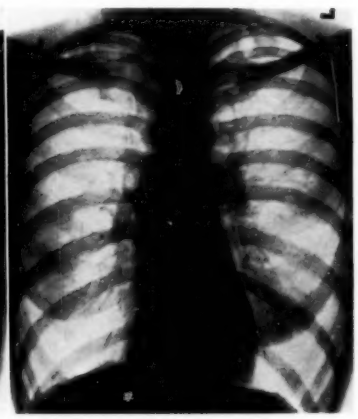


Fig. III

DR. BRAILSFORD: MYELOCELE OF THE UNBORN FŒTUS

Fig. I

Fig. II

Fig. III

Fig. IV

cellular exhaustion or degeneration, occurring during the course of the injections, may have disappeared. From the limited material at our disposal we cannot decide whether or not experimental diabetes, produced by pituitary extracts, is always accompanied by cytological changes in the beta cells of the pancreatic islets, and in this respect differs from human diabetes.

There is no evidence as to the time of onset of the hyalinisation of the islets in Dog 28. Hyalinisation is, of course, a common lesion in human diabetes. It seems likely that extra strain on islets already in a state of functional exhaustion—e.g., those of Dog 40—might be sufficient to cause extensive hyalinisation of the islet cells. The abrupt withdrawal of insulin may have contributed extra strain on the islets of Dog 28, but it is very unlikely that complete hyaline replacement could have occurred in the five days before the animal died.

The question now arises: are the islet changes sufficient in themselves to account for the diabetic condition of Dogs 28 and 40? In the case of Dog 28 there is no difficulty whatever in considering the islet lesions entirely sufficient to account for the condition of the animal. It is nevertheless very surprising to find that this animal lacked any recognisable islet tissue, yet differed so markedly from a depancreatised dog. At present there is no direct evidence that a secretion of the acinar pancreatic tissue plays a part in carbohydrate metabolism, but this possibility may have to be considered. The changes in the islets of Dog 40 were admittedly slight and not easily recognised, and this animal's pancreas contained apparently normal islet tissue. It is by no means obvious that such changes as were present were sufficient in themselves to account for the severe and persistent diabetes. On the other hand, it has already been mentioned that human diabetes is often associated with a similar lack of any profound or obvious change in the histological appearance of the islet tissue. It is perhaps of some significance that the diabetic condition of Dog 40 is apparently slightly less severe than that of the three other similar dogs so far examined. Marks and Young (1938) determined the relative amounts of sugar and nitrogen excreted when these permanently diabetic dogs received a non-carbohydrate diet. Although the D/N ratios were not far from 3/1, the value for Dog 40 was occasionally below this figure while the ratio for the other dogs was usually around 3·5/1. Moreover, although the other dogs often quantitatively excreted 50 g. of glucose added to a protein diet, Dog 40 usually excreted slightly less than the amount ingested. It must be stressed, however, that over a period of ten months Dog 40 has not shown any sign of progressive recovery from the diabetic condition, and his state was not improved after a period of insulin therapy, during which his islet cells were presumably rested.

With regard to the other endocrine glands examined (Dogs 16 and 28), we have been unable to discover any marked pathological changes which might be associated with the experimental diabetes. At present we have an insufficient number of pituitary glands from these diabetic dogs to decide whether significant changes have occurred in the glandular cells of the pars anterior and pars intermedia.

DESCRIPTIONS OF ILLUSTRATIONS ON PLATE

MR. KENDALL AND DR. THOMSON

FIG. I.—Subungual glomus tumour in Case 2.

FIG. II (same case).—Section of the tumour (low power).

FIG. III.—Subungual tumour in Case 3.

FIG. IV (same case).—Section of the tumour (low power).

DR. ELLIOTT

FIG. I (Dec. 31st, 1937).—Small pneumothorax on right side. Extensive subcutaneous emphysema. The position of the chest consistent with that seen in asthma. No other underlying lung lesion shown.

FIG. II (Jan. 14th, 1938).—Pneumothorax smaller. Still a considerable degree of surgical emphysema.

FIG. III (March 25th, 1938).—No evidence of disease of the chest.

DR. BRAILSFORD

FIG. I.—Antero-posterior view of spine of mature normal fœtus.

FIG. II.—Antero-posterior view of fœtal spine with myelocele.

FIG. III (same case).—Lateral view showing characteristic hump of myelocele in lumbar region.

FIG. IV.—Fœtus radiographed in utero, showing myelocele of lumbar spine.

SUMMARY

1. The pancreatic islets of two dogs, killed during a period of daily injections of a diabetogenic anterior pituitary extract, showed cellular proliferation and hydropic degeneration in individual islet cells.

2. The pancreas of a dog, which had been diabetic for ten months after cessation of pituitary injections, and which probably died in diabetic coma, contained no detectable normal islet tissue. The islets were completely hyalinised. Pancreatic tissue was obtained from a second dog, which had been diabetic for nearly ten months after cessation of injections, by biopsy operation during a period of insulin therapy. There were some normal islets, but the majority showed varying grades of depletion of cytoplasmic granules in the beta cells. Only very few of the islet cells of this dog exhibited hydropic degeneration.

3. One dog, the only one in six which failed to become permanently diabetic following treatment with suitable anterior pituitary extracts, had, one month after the cessation of pituitary injections, islets of Langerhans which appeared to be normal in every respect.

4. It seems possible that there are three types of response of the islet cells to the injections of anterior pituitary extract: (*a*) proliferation, (*b*) hydropic degeneration of some beta cells, (*c*) disappearance of the granules in the cytoplasm of other beta cells. Hyalinisation may finally occur. Hydropic degeneration was not a prominent feature of the islets of the two permanently diabetic dogs.

5. Proliferation of the islet cells, which was also observed in the pancreas of the rat (Richardson and Young 1937) may precede, in the dog, the exhaustive or degenerative changes which accompany the onset of permanent diabetes.

6. The other endocrine organs of those dogs in which they were examined showed no striking histological changes.

REFERENCES

Allen, F. M. (1922) *J. metab. Res.* **1**, 1.
Bailey, J. (1937) *J. Path. Bact.* **44**, 272.
Marks, H. P., and Young, F. G. (1938) *J. Physiol.* **92**, 14P.
Richardson, K. C., and Young, F. G. (1937) *Ibid*, **91**, 352.
Thomas, T. B. (1937) *Amer. J. Anat.* **62**, 31.
Warren, S. (1930) The Pathology of Diabetes Mellitus, Philadelphia.
Weichselbaum, A. (1911) *Wien. klin. Wschr.* **24**, 153.
Young, F. G. (1937) *Lancet*, **2**, 372.
— (1938a) *J. Physiol.* **92**, 15P.
— (1938b) *Biochem. J.* **32**, 513.

GLOMUS TUMOURS

By A. Wallis Kendall, M.S. Lond., F.R.C.S. Eng.
ASSISTANT SURGEON TO KING'S COLLEGE HOSPITAL, LONDON; AND

Sydney Thomson, M.D. Camb., F.R.C.P. Lond.
PHYSICIAN IN CHARGE OF THE SKIN DEPARTMENT OF THE HOSPITAL

(WITH ILLUSTRATIONS ON PLATE)

Although the existence of glomus tumours has been recognised clinically for many years, their pathogenesis has been determined only comparatively recently. It is now known that they have their origins in certain normal minute organs, the "neuro-myo-arterial glomera" of Masson. Overgrowth of the constituent parts of such a glomus results in the formation of a small tumour, with certain characteristic histological and clinical features. In the past some of these tumours have undoubtedly been mistaken for angiosarcomata or peritheliomata, whilst others have obtained scanty recognition as "painful subcutaneous tubercles."

Though glomus tumours are rare many of them certainly escape recognition and record. In the eleven years following Masson's description of the glomus in 1924 only about 65 cases were reported (Bailey 1935). But the 3 cases now to be described were seen by us within two years at one hospital, which suggests that the rarity of the condition has been over-estimated—unless the "rule of threes" be invoked.

THE GLOMUS

The work of Grant (1930) in this country has supported and amplified that of Masson, enabling us to appreciate the existence of these complex bodies. A brief summary of their main features may perhaps be permitted, as they are still but little known. The diameter of the normal glomus may be as little as 60 μ or as much as 200 μ. It is a microscopic arteriovenous anastomosis provided with a special nervous mechanism and is surrounded by loose connective tissue. Each structure is composed of an afferent artery, the anastomosis, collecting veins, and coarse lamellated connective tissue which acts as a surrounding envelope. The essential part is, of course, the anastomosis, an arteriovenous channel which is usually both coiled and twisted. This vessel is extraordinary in that the elastica interna is absent; its lumen is narrow but is yet capable of considerable dilatation, its wall is thick and contains special "glomus-cells," and finally it is surrounded by a thick network of nerve-fibres. The glomus-cells are actually unstriped muscle-fibres so modified that they appear on section as large round or oval cells with chromatin-poor nuclei and a fair amount of cytoplasm. Numerous intercellular processes connect them together.

These curious organs are found in the deepest parts of the dermis and adjacent subcutaneous tissue, usually aggregated into groups. They occur particularly over the palmar and plantar surfaces of the hands, fingers, feet, and toes, but they are absent from the dorsal surfaces except for the nail-beds, where they are very numerous indeed. It is said that the normal glomus has so far been found only in the hands and feet of human beings, but it is at least certain that glomus tumours have been recorded in other parts of the body. The organs undoubtedly play a great part in the regulation of the skin temperature in those areas where they are present. Masson suggests that they also assist in the maintenance of interstitial pressure, which must facilitate the functions of the tactile corpuscles.

THE TUMOUR

Each tumour is seen as a well-defined round or ovoid growth situated at the junction of the dermis and subcutaneous tissue and projecting into both. The lamellar capsule encloses a mass of cells in which numerous spaces are seen. These spaces are largest at the periphery, being converted into smaller fissure-like channels in the centre. Under higher magnification it can be seen that a single layer of flattened epithelial cells lines most of the spaces, and that these are themselves vascular, for the larger peripheral lumens contain blood. The majority of the cells in the tumour are the glomus-cells to which reference has already been made and which really form a syncytium of the special unstriped muscle cells of the vessel walls.

Each tumour has a definite hilum and here the afferent and efferent vessels are enclosed in connective tissue. The former vessel changes its characteristics abruptly on entering the capsule; it becomes narrow and its wall becomes thicker, being now composed of increased unstriped muscle-fibres which are more and more characteristically glomus-cells the nearer the centre of the tumour is approached. Elastic tissue is present in the periphery but has disappeared in the centre. Myelinated nerve-fibres are seen at the hilum but only unmyelinated fibres can be found within the capsule.

In brief, the glomus tumour resembles the normal glomus in structure—it is merely an overgrowth of a normal organ. Masson distinguishes three sub-varieties each distinguishable by the dominance of a particular feature. His nomenclature is self-explanatory: angiomatous, paucivascular, and lastly, neuromatous. In the paucivascular form there are more likely to be some degenerative changes and indeed columns of glomus-cells showing mucoid degeneration (stained by Athenian blue) are seen in our first case (Fig. V in text), which corresponds to Masson's paucivascular variety. In our third case the tumour is more vascular and may be classified as a representative of the angiomatous type (Fig. IV on Plate). There is no point in describing the histology of these cases in detail; all three showed the features essential to these tumours. Parkes Weber and Freudenthal, the authors of a masterly treatise on this subject (1937), have kindly examined the material from our three cases and are in complete agreement with the diagnosis in each instance. This agreement is particularly important in the first case, an example of heterotopic growth, in that the tumour appeared in a site in which normal glomera have not yet been detected.

CLINICAL FEATURES

Glomus tumours are commonest in middle age but they have been described both in young and old. In about half the recorded cases there is a history of previous trauma, a history which may sometimes be doubtful, though often, as in our first case, it seems to be irrefutable. The tumours themselves are small and purplish, the deeper examples resembling a fresh bruise whilst the more superficial lesions are somewhat redder and appear to be more frankly hæmangiomatous. They are most frequently seen in the nail-beds of the fingers but a few have been found on the trunk. By no means all of these heterotopic growths can, however, be accepted as true glomus tumours.

The dominant symptom is pain and this has usually been present for a number of years before the patient seeks relief. This painful period has averaged fourteen years in the cases which have been described previously and has ranged from five to twelve years in our series of 3. Pain may first be noticed a few months after the appearance of the discoloured tumour or its development may be delayed; but in any case it is usually only slight at first. Sooner or later however it becomes remarkably severe, with characteristic paroxysms. When the patient presents himself for treatment it is sometimes found that severe pain has been present for considerable periods. The delay in seeking relief is almost certainly to be explained by the paroxysmal and

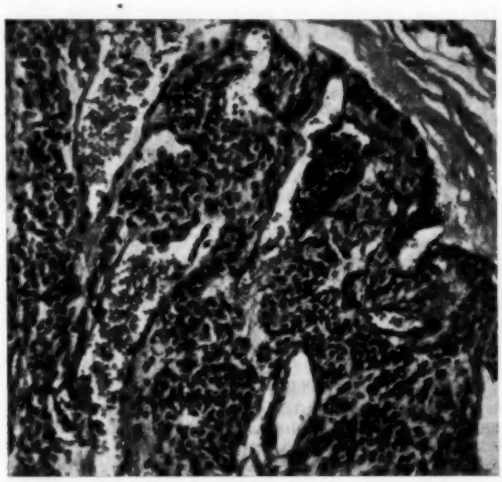


FIG. V.—Section of tumour from Case 1 showing mucoid degeneration.

inconstant nature of the pain; it provides an excellent example of the rapidity with which past discomforts are minimised and partially forgotten. The attacks are always excited by trauma, though a touch may suffice, or even a change in temperature (Case 2). The pain is most frequently burning or stabbing, and tends to radiate proximally along the affected limb. In none of our 3 cases did it wake the patient at night; it may be remarked that the patients were all normal and otherwise healthy subjects showing no signs of a neurotic tendency.

When the tumour is subungual (its most frequent site) the discoloration under the nail is usually noticed early on, being then dismissed as a painful bruise. Later the nail becomes deformed either by ridging or central elevation or sometimes by partial splitting of the nail-plate. In many such cases there will almost certainly be a history of previous avulsion of the nail without relief. By the time such a patient seeks advice he will have perfected his own protective mechanism of avoiding slight friction and knocks, and it will be found that all examination in the form of palpation is firmly discouraged.

CASE-HISTORIES

Case 1.—A bus-driver, aged 38, attended the out-patient department of King's College Hospital complaining of a painful lump just above his left knee. Ten years previously, whilst getting off his bus, he knocked this part of his knee and a small painless lump appeared after a few days and lasted about a week. About five years later he noticed at the same situation a small nodule which caused some discomfort for a few days and then again vanished. Ten days before coming to hospital he began to have a severe stabbing pain in the knee and once again noticed the small swelling which was now larger. The pain became much worse, recurring spontaneously at about two-hourly intervals during the day and returning if the part received the slightest knock. It radiated up and down the leg but was absent at night. Examination revealed a small bluish-red swelling about an inch in diameter over the upper and outer part of the left patella. Satisfactory palpation was not permitted but it was obvious that the nodule was attached to the skin and moved freely with it. The tumour was excised together with an elliptical area of skin. It was then obvious that the pink growth was adherent to the skin and was encapsulated. Subsequent measurements proved its longest diameters to be 8×9 mm. The patient was seen more than two years later and there had then been no recurrence of either tumour or symptoms.

Case 2.—A woman, aged 42, attended the out-patient department complaining of pain under the thumb-nail of the right hand. The pain had been present intermittently for twelve years but at first was not very severe. When it began the patient noticed that there was a bluish-red spot under the nail. About three years later the nail began to show a raised central ridge and ultimately split in this situation, and had been deformed ever since. The pain was worse in cold weather and with the slightest knock became extremely severe and lancinating. It radiated up the arm and even involved the right side of the face. There was no history of any definite antecedent trauma. On examination the nail was seen to be centrally ridged and split, with a reddish discoloration deep to the crescent (Fig. I). Very slight pressure on the nail caused excruciating pain. The central portion of the nail was removed and a small pinkish tumour, 4 mm. in diameter, underlying its basal portion was easily found and excised (Fig. II). The patient has been entirely free from symptoms since the operation.

Case 3.—A woman, aged 51, attended the hospital because of pain under the thumb-nail of the right hand. This had been present for five years and was mainly of an aching character except when touched or knocked, when it became very severe and radiated upwards. The nail had twice been removed within the previous twelve months (elsewhere). Temporary relief was obtained on each occasion but lasted only until the nail had regrown, when the pain returned with its old severity. There was no history of trauma. Inspection showed a deformed nail (Fig. III) having a central raised ridge with some slight hollowing on either side. At the base of the nail the centre of the nail-bed showed a pink discoloration about 2 mm. in diameter. The slightest touch to the nail excited the most intense pain. The nail was avulsed and a small rounded tumour, $4{\cdot}5 \times 3{\cdot}5$ mm. in diameter and yellowish-pink in colour, was removed from the deeper part of the nail-bed at the level of the base of the nail (Fig. IV). The nail has now completely regrown and there has been complete freedom from symptoms since the day of operation. It is interesting to note that the thumb-nail of the left hand now shows central ridging, but there are so far no signs or symptoms of an underlying glomus tumour.

SUMMARY

Glomus tumours are formed by the overgrowth of minute arteriovenous anastomoses normally found in the skin and subcutaneous tissues particularly of the hands and feet. They are most common under the

finger-nails and may give rise to severe paroxysmal pain over a period of many years.

Three cases are here recorded in which such tumours were excised, with relief of symptoms.

REFERENCES

Bailey, O. T. (1935) *Amer. J. Path.* **11**, 915.
Grant, R. T. (1930) *Heart*, **15**, 385.
Greig, D. M. (1928) *Edinb. med. J.* n.s. **35**, 565.
Masson, P. (1924) *Lyon chir.* **21**, 257.
— (1936) *Bull. Histol. Tech. micr.* **13**, 209.
Weber, F. P., and Freudenthal, W. (1937) *Brit. J. Derm.* **49**, 151.

SUBCUTANEOUS EMPHYSEMA AND PNEUMOTHORAX IN BRONCHIAL ASTHMA

BY R. W. ELLIOTT, M.Sc., M.B. Sheff.
HOUSE PHYSICIAN, ROYAL INFIRMARY, SHEFFIELD

(WITH ILLUSTRATIONS ON PLATE)

ONE might expect that in chronic asthmatics the combination of violent respiratory efforts with an emphysematous condition of the lungs would often lead to subcutaneous emphysema or a pneumothorax; but apparently it does not do so. As a complication of asthma, pneumothorax is, I believe, the less uncommon of these two accidents; but I have been able to find reports of only four cases of subcutaneous emphysema and none with a pneumothorax as well. The association must then be exceedingly rare.

CASES OF SUBCUTANEOUS EMPHYSEMA REPORTED ELSEWHERE

1. *Calverley 1902.*—A male athlete aged 17 who had had asthma for 11 years. He had an ordinary attack associated with a fit of coughing. He rested for a day and towards evening felt a pain in the chest and noticed a swelling in the neck which became larger during the night. The lower part of his neck on both sides was swollen and puffy. Respiratory sounds were easily heard in the neck, together with the typical cracklings of subcutaneous emphysema. No pneumothorax or any lesion in the lungs. No emphysema over sternum or ribs. Cardiac dullness absent. Pulse almost imperceptible during inspiration, stronger and slower during expiration.

2. *Whilby 1905.*—A man aged 25 in good general health who had had asthmatic attacks since boyhood. On the day following an ordinary attack he noticed swelling of the front and sides of his neck and this gradually extended to his face and forehead, arms, and wrists, and finally to his thorax and back as far as the sacrum. Palpation revealed the crackling of subcutaneous emphysema. Sputum was purulent and contained pyococci but no tubercle bacilli. His dyspnœa was relieved by morphia and lobelia and the emphysema, which had never been seen in any former attack, disappeared as the attack passed off.

3. *Kahn 1927.*—A girl aged 8 who had had attacks of asthma every 4–6 weeks for 6 years. During a not particularly violent attack swelling due to subcutaneous air infiltration was noticed over the upper part of the chest, back, shoulders, neck, and face, the appearance of the face suggesting parotitis. No pain. Physical signs in the lung were those of an ordinary asthmatic attack. Radiography of the chest revealed the presence of air beneath the fascial layers of the chest and neck, with no other pulmonary lesion and no indication of the site of leakage of the air. No previous similar attacks. Adrenaline injections improved the patient. The air was absorbed in 10 days.

4. *MacDermot 1929.*—A man aged 22 who had had asthmatic attacks for 6 years. During a paroxysm he felt a pain in the upper part of his chest. His neck began to swell immediately afterwards. On admission to hospital he had marked subcutaneous emphysema of the tissues of the neck extending up to the angle of the jaw and down to below the clavicles. Physical examination of the chest gave all the signs of bronchial asthma. Radiography of the chest showed no pathological lesion of the lungs but air was seen in the subcutaneous tissues. No previous attacks. Attack subsided together with the emphysema in 5–6 days. A later attack did not cause a recurrence of subcutaneous emphysema.

REPORT OF PRESENT CASE

A woman aged 46 was admitted to the Royal Infirmary, Sheffield, as an emergency on Dec. 30th, 1937. She had had pneumonia in 1918, since when she had had attacks of asthma at irregular intervals and of irregular duration, chiefly in the winter. The attacks were more troublesome at night and were always associated with cough and copious frothy sputum; no hæmoptysis. During the last three or four years she had become increasingly breathless on exertion, but previous to this had felt in perfect health between the attacks. She had had no treatment for her asthma.

On the night of Dec. 29th, 1937, whilst having her usual nightly wheezing attack, she noticed that the right side of her neck was a little swollen. The swelling gradually became bigger and involved her face and later her arms and chest. There was no pain. The attack lasted throughout the next day, and towards evening she called in her private doctor who sent her into hospital.

She was a small, rather ill-nourished woman. Her breathing typically asthmatic—rapid and wheezy with greatly prolonged expiration. The chest was mainly held in a position of inspiration. She was very distressed. Pulse shallow, 132 per min. Blood pressure 115/80 mm. Hg. Temperature normal. Both sides of the chest moved equally. There was bulging at both apices on coughing. Liver and cardiac dullnesses were both diminished. There was a wide costal angle and the whole of both sides of the chest was hyper-resonant. Expansion of the chest was only half an inch. The breath sounds were very musical over the whole of the chest with profuse râles and rhonchi. As far as could be determined clinically there was no alteration in the position of the heart. The heart sounds were very faint. There were no clinical indications of a pneumothorax.

The right side of the neck was swollen and puffy, as also was the chest, face, and right arm. The swelling gave the typical "egg-shell crackling" sensation to the touch, and crackles could be clearly heard with the stethoscope. There was definite cyanosis.

The patient was given 4 minims of adrenaline (1 in 1000) subcutaneously every three hours, but this did not improve her condition, and in the next three days she became very much worse. The emphysema gradually spread until it involved the whole of the body with the exception of the hands and the legs below the knees. The pulse became shallower and was maintained at 130–140 per min. Cyanosis continued and necessitated continuous intranasal oxygen. The face was greatly swollen, especially in the eyelids, and this rendered vision impossible. She became semi-comatose and could only be roused with difficulty. So serious was her condition that her life was despaired of. A radiographic examination of the chest was made on Dec. 31st (Fig. I on Plate). To our surprise this showed pneumothorax on the right side although there were still no clinical signs of this condition. The lung was not completely collapsed, and the position of the heart was normal.

Large reservoirs of air were seen in the subfascial planes of the chest wall.

Adrenaline and Coramine injections were given every three hours, and the patient was on continuous oxygen but her condition became worse. We were unable to account for her extreme distress. The pneumothorax was not complete and the normal position of the heart did not suggest that the distress arose from a greatly increased intrathoracic pressure. This was confirmed on Jan. 1st by introducing the needle of an artificial pneumothorax apparatus into the right pleural cavity. The average readings of the manometer oscillations showed a positive pressure of only 4–5 cm. of water. The removal of 350 c.cm. of air soon brought the readings down to a negative pressure of 2–3 cm. of water, but this made no difference to the patient's general condition.

In view of her condition another attempt to remove air from the pleural cavity was made on Jan. 2nd, but a negative pressure of 2–3 cm. of water was found and hence no air was removed. The skin over the breasts was now becoming tense, and to prevent possible gangrene of the skin, two incisions

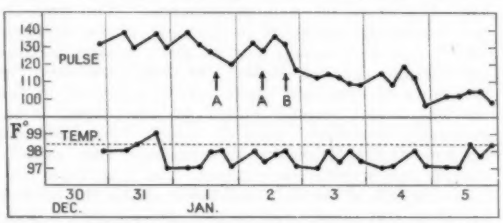


FIG. IV.—Pulse and temperature chart. A = pleural puncture. F = incision of subcutaneous tissues.

each about 2–3 in. long were made above each breast. Nothing of note happened whilst the subcutaneous tissues were being incised, but as soon as the scalpel perforated the deep fascia, air was expelled with alarming force and the tissues collapsed visibly. Within the next 24 hours the patient's condition definitely improved, her pulse slowing to 108 per min., and becoming stronger (Fig. IV). The wounds were left open to allow the escape of as much air as possible, but it is doubtful if any escaped after about two days at the most, as blood-clot and granulations were already forming in the bottom of the wound.

During the next ten days the air in the tissues gradually disappeared, the patient's general condition slowly improved, and her pulse gradually fell to normal. Radiograms taken 9 days afterwards showed that the pneumothorax was very much less in extent (Fig. II on Plate).

An interesting feature of this patient was her eyelids. As her general condition was improving she complained that she was unable to see because of her greatly swollen upper eyelids, which were tense with subcutaneous infiltration of air. Now whilst attempting to take a sample of blood for a routine examination from an arm vein I had had the inglorious experience of removing merely a syringeful of air, owing to the surrounding emphysema. I therefore decided to apply this result to the eyelids and with successful results. About 6 c.cm. of air was removed from each eyelid; they collapsed like a burst balloon, and the patient was able to see immediately afterwards. This is rather surprising because one usually thinks of subcutaneous emphysema as being widely diffused in the tissues rather than being collected in small reservoirs.

The patient was discharged from hospital after being in for a month. She was feeling very well indeed, apart from a little shortness of breath, which could be accounted for by her emphysema. She has been kept under observation ever since as an out-patient. In spite of further nocturnal attacks of asthma, she has had no recurrence of the emphysema or pneumothorax.

COMMENTS

By far the commonest cause of pneumothorax is the rupture of a tuberculous focus into the pleural cavity. Because of chronic cough and sputum this patient was kept under constant observation by the tuberculosis authorities from 1921 until 1933, repeated radiograms of the chest and sputum examinations during this period being all negative for tuberculosis. On three occasions during this period she was taken into hospital for observation, but on each occasion was discharged as being free from tuberculosis. Radiograms during her recent attendance at the Royal Infirmary showed no evidence of disease of the lungs, nor was there any clinical evidence of tuberculosis (Fig. III on Plate).

Although it is always difficult to exclude tuberculosis with certainty, there seems to be no evidence for making such a diagnosis in this patient, and it seems justifiable to conclude that the present case was one of chronic bronchitis with asthma. Several members of her family were also sufferers from bronchial asthma.

In the other reported cases, as in this, subcutaneous emphysema occurred only after attacks of asthma had been present for many years, suggesting some gradual change in the pulmonary tissues which finally gives way under the great strain. On the other hand, one would then expect repeated attacks of emphysema once these had begun, whereas in none of the cases was a second attack reported. The previous cases were all young—8, 17, 25, and 22 years respectively—so that the present patient deviates somewhat in this respect in being 46. It is interesting to note in this connexion that the so-called spontaneous or idiopathic pneumothorax is common in young "healthy" persons. This suggests that rupture of the air cells in these cases is mechanical rather than pathological.

In the present case the pneumothorax does not seem to have been the cause of the patient's distress, since the air in the pleural cavity was not under sufficient pressure, and release of the slight tension did not improve matters. Release of the tension of air in the tissues, however, seemed to produce a definite change for the better. I do not pretend to understand the significance of this, but the fall of the pulse-rate to normal after the incisions were made suggests that back-pressure (possibly on the mediastinum) caused some degree of cardiac embarrassment. In none of the other cases was the patient's general condition bad enough to cause anxiety, and no treatment was necessary apart from that of the primary asthma. Here the patient was desperately ill, and although the above treatment was carried out with no obvious rationale it had the desired results.

TENTATIVE SUGGESTIONS

Boyd (1935) describes a condition of interstitial emphysema of the lung in children caused by over-distension and rupture of the alveoli which may arise from the violent coughing of whooping-cough, the air escaping into the interstitial tissues of the lung. The air collects in the lymphatics in the form of tiny beads, being seen particularly well under the pleura. The air may pass along the lymphatics to the mediastinum, and from there to the root of the neck. If such an occurrence is possible, may we not invoke this pathology in these non-fatal cases of asthma where post-mortem specimens have not been obtainable? In favour of this suggestion we have the fact that in all these cases the emphysema was noticed first just above the clavicles on one or other side, and from this point spread for a varying distance in the tissues, suggesting a rise of air from the mediastinum.

We have now to attempt to find a common cause for the pneumothorax and the subcutaneous emphysema in this case. Miller, quoted by Boyd, has described a condition, closely related to interstitial emphysema, in which the air escaping from a ruptured alveolus separates the pleura from the underlying lung in much the same way as the escaping blood in a dissecting aneurysm separates the coats of an artery. This causes a small bleb on the surface of the lung. Rupture of this bleb would naturally give rise to a pneumothorax, and at the same time allow the air to enter the interstitial lymphatics and spread thence to the mediastinum and root of the neck. If such was the mechanism in the present case one would not expect the air in the tissues to be under pressure as it seemed to be, unless some valvular mechanism was at work.

When first seen the patient did not show much cardiac embarrassment. The distress gradually developed in about four days during her stay in hospital, suggesting a gradual increase in the tension of the escaping air. This is quite in accordance with the effect of the incisions which released the tension, because although an immediate effect was seen, the pulse-rate and pulse strength took several days to return to within normal limits. Hence whatever mechanism was involved, it was slow in creating an effective disabling pressure.

I am indebted to Dr. R. Platt for his permission to record this case and for his criticism and suggestions.

REFERENCES

Boyd, W. (1935) Pathology of Internal Diseases, Philadelphia.
Calverley, J. E. G. (1902) *Brit. med. J.* **2**, 1899.
Kahn, I. S. (1927) *J. Amer. med. Ass.* **88**, 1883.
MacDermot, H. E. (1929) *Canad. med. Ass. J.* **21**, 708.
Whitby, C. J. (1905) *Brit. med. J.* **1**, 73.

RADIOGRAPHIC DETECTION OF MYELOCELE OF THE UNBORN FŒTUS*

BY JAMES F. BRAILSFORD, M.D., Ph.D. Birm., M.R.C.P. Lond.

HON. RADIOLOGIST, THE QUEEN'S HOSPITAL, BIRMINGHAM

(WITH ILLUSTRATIONS ON PLATE)

RADIOGRAPHY is the most valuable method available to the obstetrician for the diagnosis of deformities of the unborn fœtus. It already permits of the early recognition of gross deformities such as double monsters, anencephaly, hydrocephaly, and severe spinal deformities, and with increasing refinement of technique it should reveal some of the lesser, though important, developmental deformities. My purpose in this paper is to set forth the radiographic characters of one such deformity, the myelocele, which, though incompatible with life, is undetectable by clinical methods.

RADIOGRAPHIC APPEARANCE OF THE NORMAL FŒTAL SPINE

On lateral projection the normal fœtal spine near maturity shows a uniform kyphosis which embraces the cervical, dorsal, and lumbar vertebræ. In the lumbosacral area the general curvature ceases, for the sacrum is flattened out and directed slightly backward. The vertebral bodies show a very gradual increase in size from the cervical to the lower lumbar region and then a diminution to the terminal sacral segments. The dorsal vertebral bodies at this stage often present a bobbin-shaped appearance due to incomplete ossification of their middle third. The bodies of the upper two or three lumbar vertebræ may also show a notch in the middle of their anterior and posterior surfaces whereas those of the lower two are more completely ossified and have a regular contour. The length of the pedicles appears to be equal to the antero-posterior measurement of the bodies, and the articular processes, particularly the inferior, continue the backward projection and increase the antero-posterior dimension of the vertebræ to about twice that of the bodies.

On the antero-posterior projection (Fig. I on Plate) the vertebral bodies show a gradual increase in width and a slighter increase in depth from the upper cervical to the lower lumbar regions, followed by a more rapid diminution in size to the lower sacral level. The bodies, which are oval in shape with often a slight notch in the middle of their superior and inferior surfaces, appear to be pierced by two small holes, one on each side slightly away from the midline—the so-called venous channels. The pedicles and laminæ are projected in the plane of the vertebral bodies and the laminæ almost meet in the midline posteriorly. The articular processes are seen as two rows of opacities which are wider apart in the cervical area, become closer in the dorsal area, gradually separate again to reach their cervical distance at the first sacral vertebra, and then rapidly narrow and become less distinct. The transverse processes appear as small lateral tubercles on the lumbar vertebræ but show greater and more characteristic development in the dorsal area.

RADIOGRAPHIC APPEARANCE OF THE MYELOCELE

On lateral projection the position of the myelocele is indicated by a break in the normal backward curvature and the appearance of a rounded kyphos or hump which includes about six vertebral bodies (Fig. II). The developmental defect produces a bow-like deformity of the spine resembling in shape the bowing associated with projection of the fifth lumbar vertebra which I described as characteristic of spondylolisthesis (Brailsford 1935a and b.) This characteristic bow-like projection, which may be the only indication of the myelocele, depends on the arrest of development of the neural groove. Normally the neural folds meet and fuse, and the neural canal becomes completely encased in bone developed by ossification of the primitive vertebral bow to which the vertebral musculature is attached. In myelocele the neural folds remain apart but their cellular elements undergo progressive differentiation and development which gradually widens the breach in the midline and thus prevents apposition of the articular processes of adjacent vertebræ and allows the deformity to take place. In this kyphotic area the radiographs show little or no development of the laminæ or processes.

On antero-posterior projection (Fig. III) the defect may be recognised by the lateral displacement and direction of the pedicles and processes, which are projected on either side of the adjacent vertebral bodies and not behind as in the normal spine. The total length of the affected spine is diminished, the amount of the diminution depending on the degree and extent of the defects. One or more of the vertebral bodies may exhibit two unfused ossific nuclei. In severe cases defects may be present throughout the entire length of the spine and may be associated with anencephaly or hydrocephalus. In these cases the vertebral bodies do not show the normal uniform progression and the cervical and upper dorsal bodies

* Part of a paper read before the Midland Obstetrical Society in May, 1937.

may be small while the lumbar appear unduly large and deep in comparison.

The following case (for the clinical details of which I am indebted to Mr. Selby Tait) is one in which the radiographic evidence solely led to early detection of the defective development and indicated the essential treatment.

A primipara aged 23. Amenorrhœa from July 31st, 1936. Admitted to hospital Feb. 24th, 1937. No abnormal antenatal symptoms or signs. Breech presentation was suspected. Radiographs (Fig. IV) showed breech presentation with the characteristic "hump" of a myelocele. Premature labour was induced and the presence of a myelocele confirmed.

Since the reading of this paper the accuracy of this new sign has been verified in several cases.

SUMMARY

Myelocele is a deformity incompatible with life. It can be recognised in the unborn fœtus as a rounded kyphos or hump which includes about six vertebral bodies.

REFERENCES

Brailsford, J. F. (1935a) The Radiology of Bones and Joints, 2ED. London.
— (1935b) *Bgham med. Rev.* **10**, 82.

CUTANEOUS APPLICATION OF FOLLICULAR HORMONE

BY PROF. BERNHARD ZONDEK, M.D.

(*From the Gynæcological and Obstetrical Department of the Rothschild-Hadassah Hospital, Jerusalem*)

As I reported in 1929 the follicular hormone (œstrone) is absorbed through the skin. If we rub a hormone ointment or a hormone oil into the shaven skin of the back of a castrated mouse the animal goes into œstrus, but to obtain this effect we need seven times as much hormone as with subcutaneous injection.

The mammæ show a greater response to percutaneous hormone treatment than the uterus and vagina (Zondek 1935a). If we rub a hormone ointment into the skin of the mammary region of a male guinea-pig, first the treated and then the untreated mamma enlarges, and finally the gland secretes milk. This mammary effect can be induced with the same dose of hormone, either percutaneous or subcutaneous. These results have been verified by Jadassohn, Uehlinger, and Zuercher (1937) who, from the fact that the locally treated mammæ show a quicker and greater enlargement of the nipples than the non-treated ones, conclude that there must be a local hormonal effect. I have given the hormone percutaneously to women, using the Œstroglandol ointment kindly supplied me by Hoffmann-La Roche, and containing 1000 M.U. per gramme (Zondek 1935b). I proposed the application of this ointment in pruritus vulvæ senilis on the assumption that this painful affection could be improved by hyperæmia and softening of the tissues and found it of considerable value. I also used it in the treatment of acne vulgaris in young girls and in women at the menopause, and have been able to benefit the so-called arthritis ovaripriva of the menopause by local treatment of the joints with œstroglandol ointment, a method which deserves further trial (Zondek 1935b).

Animal Experiments

Recent investigations have shown that under certain conditions the percutaneous dose of hormone required to induce œstrus is no greater than the subcutaneous. The decisive factor is the solvent. The more readily the solvent is absorbed through the skin, the better the œstrogenic hormone can exert its effect. If the hormone is dissolved in an oil or ointment only one-seventh is absorbed through the skin; but in an organic solvent such as benzol, ether, or alcohol the whole is absorbed.

EFFECT UPON ŒSTRUS

Three groups of castrated mice received three doses of œstrone totalling 0·1–0·3 µg. (0·0001–0·0003 mg.) in 24 hours.

In *Group A* an oily solution was given subcutaneously. These animals went into œstrus.

In *Group B* a solution in olive oil was rubbed into the shaven skin of the back. These animals did not go into œstrus.

In *Group C* the œstrone was in an organic solvent (benzol or ether or 96 per cent. alcohol) and was rubbed into the shaven skin of the back. Every one of these animals went into œstrus.

EXPERIMENTS ON MALE ANIMALS

As I reported previously (Zondek 1935a) we can produce an antimasculine effect—i.e., impairment of growth of the testes—by percutaneous application of hormone ointment. If a hormone ointment is rubbed into the skin of the back of a male guinea-pig (100 M.U. per diem) for 8 days, the testes decrease in weight by 40 per cent. The antimasculine effect shows itself in the first days of treatment and gradually increases. With 36 days' treatment (a total of 2700 M.U.) the weight of the testes decreases from 3 to 1·3 g.—i.e., by nearly 60 per cent. The effect varies greatly however in different animals.

More recently we have investigated the behaviour of male rats treated for several months with œstrogenic hormone. The animals were divided into three series. The first was treated subcutaneously with the hormone in an oily solution, the second percutaneously with an oily solution, and the third percutaneously with the hormone in an organic solvent (benzol). We used animals aged five weeks weighing 40–50 g. and gave them 500 M.U. of œstrone or œstradiol benzoate twice a week. Two degrees of the antimasculine effect can readily be distinguished: (1) the testes diminish in size, and (2) they retract from the scrotal sac into the abdominal cavity. In all the three series there was atrophy of the testes, but there were differences in the degree of retraction. All the animals treated percutaneously with œstrone or œstradiol benzoate in benzol showed retraction whereas those treated percutaneously with hormone in oily solution showed only atrophy. The animals treated subcutaneously showed an intermediate effect; in most the testes were retracted but in some they remained in the scrotal sac. These results demonstrate the striking fact that the antimasculine effect of œstrogenic hormone given percutaneously in an organic solvent is equal or even superior to that of the hormone given subcutaneously.

I have since observed that also androgenic hormone given percutaneously in an organic solvent is more readily absorbed through the skin than in an oily solvent. I shall report on this elsewhere.

GROWTH IMPAIRMENT

In recent years I have studied the impairment of the anterior pituitary functions by protracted treatment with œstrogenic hormone, the most striking result being the elimination of the growth hormone and the impairment of the growth of the skeleton

and organs. I have already reported that by percutaneous administration of œstrone we can partially eliminate the anterior lobe (Zondek 1936 and 1937). The shaven skin of the back of male and female rats was painted with two drops of a solution of œstradiol benzoate in benzol three times a week—a total weekly dose of 10,000 M.U. All the animals thus treated were backward in growth. After 11 weeks' treatment their average weight was 89 g. whereas controls weighed 152 g., a difference of 40 per cent.

In our present investigations we have compared the growth impairment when the same amount of hormone is administered (*a*) subcutaneously, (*b*) percutaneously in oily solution, and (*c*) percutaneously in benzol or another organic solvent. In these experiments much smaller doses of hormone were used to ascertain which kind of treatment had the earliest effect. The animals each received 500 M.U. of œstrone twice a week. After 9 months' treatment those treated subcutaneously with the oily solution and those treated percutaneously with the benzol solution showed similar growth impairment, whereas those treated percutaneously with an oily solution showed none. As regards impairment of growth then, the solvent again plays a decisive part.

PITUITARY TUMOURS INDUCED BY ŒSTROGENIC HORMONE

As reported elsewhere (Zondek 1936 and 1937) we can produce large tumours in the pituitary glands of rats by 7 months' administration of œstrogenic hormone, and I have at my disposal 28 such tumours. In those experiments we succeeded three times in producing very large pituitary tumours by percutaneous administration of relatively small doses of œstradiol benzoate dissolved in benzol. The animals had at the same time been rubbed with benzpyrene (2 drops of a 1 per cent. benzol solution three times a week), and this might have increased the effect of the œstradiol benzoate. I therefore arranged a new series of experiments with 12 female rats aged four weeks and weighing about 30 g. The animals each received 500 M.U. of œstradiol benzoate twice a week. Four of them received an oily solution of hormone subcutaneously, four an oily solution percutaneously, and four a solution in benzol percutaneously. After 9 months' treatment I found only one pituitary tumour, and this was in a female treated percutaneously with œstradiol benzoate in benzol. In this experiment, therefore, œstrin given in an organic solvent had more effect upon the pituitary gland than the same amount of hormone dissolved in oil. Moreover the hormone dissolved in benzol and applied to the skin seemed even more effective than the hormone injected subcutaneously in oil.

Clinical Application in Amenorrhœa

To induce true menstruation after oöphorectomy it is necessary to give progesterone as well as œstrone. Unfortunately, though the two hormones closely resemble one another chemically and are both easily soluble in organic solvents, progesterone is not so readily absorbed through the skin as œstrone. This was shown in young rabbits which were given œstrone for eight days followed by progesterone rubbed into the skin of their back for five days. Their uteri showed progestational changes, but these were less than if the hormone had been injected. Since progesterone is still very expensive, injection is to be preferred until a cheaper preparation is available.

The experiments on animals were carried out with œstrogenic hormone dissolved in benzol. In women an alcoholic œstrone tincture (96 per cent. alcohol) proved best. I used the tincture in the following strengths:—

(*a*) Tinctures containing 3 mg. of œstrone—i.e., 30,000 mouse units—in 1 c.cm. Patients were ordered to drop 20 drops (0·5 c.cm.) upon the hairless skin of the forearm or front of the thigh morning and evening for twenty days and to rub with the forefinger until it had completely disappeared. The total dose was 600,000 M.U.

(*b*) Tinctures containing 0·2–0·3 mg. (2000–3000 M.U.) of œstrone or œstradiol benzoate in 1 c.cm. The dose was 5 c.cm. of this tincture (200 drops) rubbed into the skin twice daily for twenty days, a total dose of 400,000 to 600,000 M.U.

(*c*) Tinctures containing 10 mg. (10,000 M.U.) of œstradiol benzoate per 1 c.cm. The tincture was rubbed into the skin 8 to 10 times in twenty days, each dose being 5 c.cm. (50,000 M.U.), and the total dose 400,000 to 500,000 M.U.

After the percutaneous treatment with œstrogenic hormone intramuscular injections of 8–10 rabbit units of progesterone were given daily for five days (total 40–50 units).

I have an impression that the tincture of œstrone is more effective than that of œstradiol benzoate. Rubbing in 5 c.cm. (2000 to 3000 M.U. per c.cm.) of an œstrone solution twice a day appears to be the best method.

CLINICAL RESULTS

Percutaneous treatment with hormone tincture has now been given to 12 patients in 18 menstrual cycles. Bleeding was induced 10 times. It should be emphasised that injections of hormone are not always successful; thus in Case 7 the subcutaneous administration of 400,000 M.U. of œstradiol benzoate and 40 rabbit units of progesterone did not produce menstruation. That we succeeded 10 times by merely rubbing the tincture into the skin appears to me remarkable. In 3 of our 8 failures menstruation was later induced by injections of hormone, so that the percutaneous route seems still to be somewhat inferior to the subcutaneous; but its simplicity makes it very agreeable to the patient, especially where treatment has to be continued permanently.

Primary amenorrhœa.—Since the results in primary amenorrhœa were most instructive I shall describe in detail the two cases treated.

CASE 1.—Aged 28. She has been married for five years and has never menstruated. In March, 1935, when treatment began, her uterus was hypoplastic and only 3 cm. long; her vagina was pale and atrophic like that of an old woman; and the urine contained prolan A (111 M.U. per litre of morning urine), indicating a severe functional disturbance. She received 450,000 M.U. of œstradiol benzoate (Dimenformon) intramuscularly followed by 25 rabbit units of progesterone. Four days after the treatment ended she menstruated for the first time in her life. The uterus then was 6·5 cm. long and its mucous membrane showed the beginning of a progestational stage without glycogen. She was treated several times in this way and regularly reacted by bleeding; but even by increasing the dose of progesterone we could not produce a normal premenstrual mucous membrane. The patient, who came from abroad, interrupted the treatment for two years, during which there was no menstruation. After this interval percutaneous œstrone was tried as follows:—

First course.—From July 28th to August 16th, 1937, she rubbed 20 drops (15,000 M.U.) of alcoholic œstrone tincture into the skin of her forearm and

SECONDARY AMENORRHŒA: RESULTS IN TEN CASES

Case.	Age.	Duration of amenorrhœa (years).	Uterus (length).	Œstrogenic hormone (M.U. twice daily) percutaneous.	Progesterone (R.U. daily).	Total dose—		Results.
						Œstrogenic hormone (percutaneous), M.U.	Progesterone (parenteral), R.U.	
3	36	3	Retroverted, 6 cm., narrow.	(*a*) 30,000 Œ.	7·5 (4 days). 10·0 (1 day).	600,000 Œ.	40	Bleeding.
				(*b*) 20,000 Œ.	7·5 (4 days). 10·0 (1 day).	400,000 Œ.	40	"
4	43	2½	7 cm.	10,000 Œ.	..	400,000 Œ.	..	"
5	39	1½	Retroverted, 7 cm., narrow.	(*a*) 10,000 Œ.	..	400,000 Œ.	..	No bleeding.
				(*b*) 10,000 Œ.	10·0 (5 days).	400,000 Œ.	50	Bleeding.
6	24	1	Very small, 3–4 cm.	(*a*) 10,000 Œ.	..	400,000 Œ.	..	No bleeding.
				(*b*) 10,000 Œ.	10·0 (5 days).	400,000 Œ.	50	Bleeding.
7	29	1½	Body hypoplastic, 6 cm.	15,000 Œ.	7·5 (4 days). 10·0 (2 days).	600,000 Œ.	50	No bleeding.
8	27	1½	Hypoplasia of third degree.	10,000 Œ.	5·0 (5 days).	400,000 Œ.	25	Bleeding.
9	28	8	4–5 cm., very narrow.	12,500 O.B.	..	500,000 O.B.	..	No bleeding.
10	34	14	6·5 cm., body narrow.	12,500 O.B.	10·0 (5 days).	500,000 O.B.	50	"
11	21	½	4 cm., body size of nut.	12,500 Œ.	..	500,000 Œ.	..	"
12	20	2	Size of finger, hypoplasia of third degree.	12,500 Œ.	10·0 (5 days).	500,000 Œ.	50	Bleeding.

Œ. = œstrone. O.B. = œstradiol benzoate. M.U. = mouse units. R.U. = rabbit units. .. = untreated.

thigh morning and evening, a total of 600,000 M.U. From August 17th to 21st she received 40 rabbit units of progesterone intramuscularly. Four days later fairly copious bleeding started and persisted for three days. Histological examination of a strip of the uterine mucosa showed the mucous membrane in the interval stage.

Second course.—From Sept. 5th to 25th the patient rubbed 5 c.cm. (15,000 M.U.) of an alcoholic œstrone tincture into her skin morning and evening, a total of 600,000 M.U.. and from Sept. 25th to 29th she received 8 rabbit units of progesterone intramuscularly daily, a total of 40 units. On the morning of Oct. 3rd bleeding began; six hours later a piece of uterine mucosa showed abundant glands but no typical progestational change.

Third course.—An alcoholic tincture of œstradiol benzoate was now given in place of œstrone. From Oct. 8th to 28th 5 c.cm. (15,000 M.U.) of this tincture was rubbed into the skin twice daily, a total of 600,000 M.U. From Oct. 28th to Nov. 1st 10 rabbit units of progesterone were injected daily intramuscularly, a total of 50 units. Four days later bleeding started and continued for four days.

In this case we were able to replace parenteral œstrone by percutaneous treatment in three successive menstrual cycles. The patient was much impressed by the method, for she was now only dependent upon the doctor for progesterone injections.

CASE 2.—A woman of 29 who had never menstruated. Her uterus was hypoplastic and narrow, but 6 cm. long. She received 5 c.cm. (15,000 M.U.) of an alcoholic tincture of œstradiol benzoate percutaneously twice daily, 60,000 M.U. in all. Subsequently 10 rabbit units of progesterone were rubbed into the skin daily for five days. No bleeding occurred. This failure could perhaps be ascribed to the fact that progesterone was given percutaneously rather than intramuscularly.

Secondary amenorrhœa.—As shown in the accompanying Table we treated 10 cases of secondary amenorrhœa varying in duration from one to fourteen years. Only cases with a severe functional disturbance were chosen, to lessen the likelihood of accidental successes. In 13 menstrual cycles bleeding was induced 7 times. The following are examples:—

CASE 3.—A woman aged 36 who had not menstruated for three years. Here we succeeded twice in producing bleeding with percutaneous treatment. The dose of œstrone in the first cycle was 600,000 M.U. and in the second 400,000 M.U. In the first cycle the mucous membrane showed glandular hyperplasia, which was probably due to 600,000 M.U. being too large a dose even when given percutaneously. A dose of 400,000 M.U. is generally sufficient.

CASE 5.—In the first cycle œstrone only was used, 400,000 M.U. of the tincture being given in twenty days, and there was no bleeding. Then a similar dose of œstrone was given followed by 50 rabbit units of progesterone intramuscularly and bleeding began. This suggests that œstrone treatment is more likely to be successful if it is followed by corpus luteum hormone. It should be emphasised, however, that here again premenstrual changes in the mucous membrane were absent.

Case 6 again demonstrates that œstrone will not induce menstruation unless it is followed by progesterone intramuscularly. In Cases 9 and 11 bleeding could not be brought on by percutaneous treatment with 500,000 M.U. of œstrone and œstradiol benzoate. In contrast to these, in Case 12 percutaneous œstrone followed by the injection of progesterone was successful.*

DISCUSSION

Experiment has shown that œstrogenic hormone dissolved in benzol, ether, or alcohol is completely absorbed through the skin, and clinical observation proves that alcoholic tinctures given in this way are of therapeutic value. Their use has the advantage that the patients are no longer dependent upon injections given by a doctor and can easily treat themselves—a considerable relief to their minds.

* I have since observed another case of secondary amenorrhœa which has shown bleeding from a proliferative endometrium after having received 400,000 M.U. of œstrone tincture percutaneously without subsequent progesterone treatment.

My experience so far suggests that success is most likely in amenorrhœa if one gives 50 rabbit units of progesterone by injection after 20 days' percutaneous treatment with œstrogenic hormone (400,000 M.U.). It is remarkable that there may be bleeding without the mucous membrane showing the typical picture of the premenstrual phase. I have noticed this also in cases receiving injections of œstrone and progesterone and have formed a new idea of the mechanism of menstruation which I shall report elsewhere. For the patient it is quite irrelevant how the mucous membrane looks—whether she bleeds from a proliferative or a progestational mucosa; whether there is pseudomenstruation or menstruation. It is only important that she does bleed, and since this is attained by simple and "natural" means she can throw off her feeling of inferiority and the subjective disturbances resulting from her missing ovarian functions.

Local treatment with hormone tincture is also worthy of consideration, particularly in arthritis ovaripriva. I have not been able to use it in acne vulgaris and pruritus vulvæ because of the irritation it may produce.

SUMMARY

The œstrogenic hormone is absorbed through the skin, but if it is applied in an oil or ointment the dose needed to produce œstrus in castrated mice is seven times as great as the dose needed when it is injected subcutaneously.

If the hormone is dissolved in benzol, ether, or 96 per cent. alcohol, it is much more readily absorbed through the skin.

A dose of œstrogenic hormone given in this way is just as effective as the same dose injected subcutaneously.

The equal effectiveness of percutaneous application in a suitable solvent has been shown by experiments in which œstrogenic hormone was used to produce œstrus in mice, to reduce the growth of the testes of rats, to inhibit the growth of young rats, and to produce a pituitary tumour in the rat.

In gynæcological practice injections of œstrogenic hormone can be partly replaced by percutaneous applications of alcoholic tincture of œstrone. Progesterone also is absorbed by the skin, but it will have to be injected until it is less expensive, for larger doses are required for percutaneous than subcutaneous administration.

Application of œstrogenic hormone to the skin, followed by the injection of progesterone, will produce uterine bleeding in primary and secondary amenorrhœa.

The rubbing of alcoholic tincture of œstrogenic hormone into the skin is almost as effective clinically as injections of the hormone, but some patients who do not react to percutaneous treatment will nevertheless react to injections.

I am indebted to Dr. M. Tausk (Organon, Oss) for kindly supplying the œstrone (Folliculin-Menformon) and œstradiol benzoate (Dimenformon).

REFERENCES

Jadassohn, H., Uehlinger, E., and Zuercher, W. (1937) *Helv. med. Acta*, **4**, 199; (1937) *Klin. Wschr.* **9**, 313.
Zondek, B. (1929) *Klin. Wschr.* **48**, 2229.
— (1935a) Hormone d. Ovariums u.d. Hypophysenvorderlappens, Vienna, p. 104.
— (1935b) *Schweiz. med. Wschr.* **49**, 1168.
— (1936) *Lancet*, **2**, 842.
— (1937) *Folia clin. orient.* **1**, 1.

VITAMIN A AND CAROTINOIDS IN BLOOD

DEFICIENCIES IN CHILDREN SUFFERING FROM XEROPHTHALMIA

BY J. H. DE HAAS, M.D.

AND

O. MEULEMANS, Chem. Eng.

(From the Children's Department of the Medical College at Batavia)

No observations have been recorded on the vitamin-A or carotene content of the blood of children suffering from xerophthalmia. The observations in this paper have been made on the blood-serum of 11 infants (7 native and 4 Chinese) and 16 young children (15 native and 1 Chinese) that were treated in our department between February and May, 1937. The diagnosis of xerophthalmia in every instance was supported in the ophthalmic department by Prof. Mulock Houwer and Dr. Sie Boen Lian.

Among the poorly fed groups of the population in the tropics, infants and young children with xerophthalmia are being constantly noticed. The peculiarity in the children here to be described, however, lies in the fact that the amount both of vitamin A and of carotinoids in their blood has been determined, after it had become apparent that an exact determination is possible with as little as 6–10 c.cm. of blood.

The method is the same as that now in use at the Hygiene Laboratory in Utrecht (Wolff 1936). It consists of saponifying the serum; shaking it with peroxide-free ether; determining the carotinoids; drying over sodium sulphate and evaporating with a current of carbon dioxide; applying Carr and Price's reaction; and determining the blue tint in the Lovibond tintometer.

In the early part of this investigation a few blood samples were examined according to the method originally used in Utrecht (van Eekelen 1931, Menken 1932, 1934), which one of us had had the opportunity of studying there. The difference between the old and the new method is of minor import.

The age of the 11 infants examined, practically every one of which was dystrophic, varied between 7 weeks and 9 months. Of these 11 infants 6 were fed with sweetened skimmed milk, 3 were breast-fed, and 2 had been fed with sweetened condensed milk, not skimmed but possibly too greatly diluted.

Of the 3 blinded infants 1 was breast-fed. The European waste product, sweetened skimmed milk, was responsible for the other 2 cases of blindness (de Haas and Meulemans 1937). The remaining 8—of whom 2 were breast-fed, 4 received sweetened skimmed milk, and 2 too greatly diluted sweetened condensed milk—suffered from a xerosis of the conjunctiva and cornea, with or without the Bitot spots; they could still be treated in time. Such a cruel incident as that by which a mother through her own breast-feeding caused blindness in her child has therefore actually occurred once amongst these infants.

INVESTIGATIONS

In 6 of these 11 infants there was no vitamin A in the blood, and in 3 of the rest only very little—

4, 6, and 8 international units* (I.U.) per 100 c.cm. of serum. On the other hand, in a Chinese female infant, 7 months old, who had been breast-fed for a month, after which she had been given sweetened skimmed milk with banana and orange juice, 31 I.U. of vitamin A were found on the day before she died of extensive tuberculosis. In a native infant aged 9 months, with perforated corneæ, breast-fed for three weeks, after which he had been fed with sweetened skimmed milk, 22 I.U. per 100 c.cm. of serum was found.

The carotinoid content (without further differentiation) in these 11 infants varied between 12 γ and 56 γ per 100 c.cm. of serum, so that in all instances it was fairly low. Actually the carotene content is still lower, seeing that the chromatographical analysis of the carotinoids was not made. In this investigation the emphasis has been laid upon the determination of the vitamin-A content in the blood, because it is likely to be a more representative measure than is the carotinoid content for determining any deficiency.

In 2 out of the 3 breast-fed infants the mothers' milk did not contain any vitamin A, whilst in the third infant (7 weeks old) there was 14 I.U., the blood of the mother containing 18 I.U. The carotinoid content of the blood of these breast-fed infants varied between 13 γ and 41 γ, in the blood of the mothers it was 18–53 γ, and in the mothers' milk 3–17 γ (all of these per 100 c.cm. of serum). For the average content of vitamin A and carotene in human and in cow's milk reference may be had to our previous publications on these subjects (Meulemans and de Haas 1936, 1938). The figures (Batavia) may be summarised as follows :—

—	International units per 100 c.cm.	
	Vitamin A.	Carotenes.
Cow's milk	±50	±20
Human milk—		
Native and Chinese..	±60	±15
European	150–200	±25

Of the 16 older children (15 native and 1 Chinese), practically all were more or less dystrophic, as is usual here amongst Chinese and native children; except for one aged 7 they were all between 1 and 4 years.

Of the 16, 13 children had been breast-fed during the first year of their life, and of the 3 bottle-fed one had been given diluted fresh milk, one had been fed with sweetened condensed unskimmed milk, and the third with sweetened skimmed milk. After the breast-feeding or the bottle-feeding these children had been fed on rice, vegetables, and a little dried fish, with few secondary adjuncts or none, this being the usual food of the young native child.

Of these 16 children one was totally blind, and two of them half blind. The others exhibited only xerosis and Bitot's spots.

In 13 of these 16 children suffering from xerophthalmia no vitamin A was found in the blood, and the other 3 had 2, 14, and 38 I.U. per 100 c.cm. of serum. No explanation could be found for this relatively high value. The carotinoid contents varied between 8 μg. and 29 μg. per 100 c.cm. of serum.

* Wolff (1936) gives the averages for the vitamin-A contents of the blood-serum in adults the following values: 90–120 I.U. = good; 45–90 I.U. = satisfactory; less than 45 I.U. per 100 c.cm. of blood-serum = insufficient. These values are 1½ times as large as those indicated in the original publication, because the conversion factor of Lovibond "blue units" into international units, which hitherto had been taken to be 4·2, according to a subsequent publication issued by the Hygiene laboratory at Utrecht, is actually 6·4 (van Eekelen, Emmerie, and Wolff 1937). In this article the latter factor is being used in converting the vitamin-A contents into I.U.

METHOD OF TREATMENT

The infants and the other children suffering from xerophthalmia, immediately upon being admitted, were given, besides an adequate diet, subcutaneously 0·5 c.cm. of Davitamon A (Organon) which contains 40,000 I.U. per c.cm., in addition to a continuous daily treatment with cod-liver oil.

If the corneæ are not as yet perforated, practically in every instance a successful result is obtained by means of this treatment, even if no vitamin A be present in the blood. In the course of treatment not a single eye was lost that had not already previously been destroyed.

After treatment the vitamin-A content of the blood increases more or less rapidly, but this, together with various other details not yet indicated here, will be described in a subsequent paper. For the present it may be pointed out that in sick dystrophic children that do not yet exhibit xerophthalmia it may happen that no vitamin A is found in the blood, so that from this communication it may only be concluded that the absence of vitamin A in the serum of children is essential but not necessarily pathognomonic for xerophthalmia.

SUMMARY

1. In infants and young children with xerophthalmia there is as a rule no vitamin A in the blood-serum; sometimes there is a little, and in exceptional cases a trifle more.

2. The carotinoid content of the blood in these cases is also low. The vitamin-A content, however, is more representative than this in judging any A-deficiency.

3. If the cornea has not yet perforated, even though temporarily no vitamin A is found in the blood, treatment with vitamin-A preparations will succeed in relieving the eye affection.

4. Sweetened skimmed milk is an "ideal" food for providing xerophthalmia in bottle-fed infants; the disease is rarely caused by other milk preparations.

5. Xerophthalmia and the practically total absence of vitamin A in the blood has also been met with in *breast-fed* infants, in which case there is in the mother's milk little or no vitamin A, and only a small amount of carotene.

This investigation has been carried out with the support of the Institution for Nutrition Research at Batavia.

REFERENCES

van Eekelen, M. (1931) *Acta brev. neerl. physiol.* **1**, 65.
— and Emmerie, A. (1935) *Ibid.* **4**, 171.
— — and Wolff, L. K. (1937) *Z. Vitaminforsch.* **6**, 159.
de Haas, J. H., and Meulemans, O. (1937) *Publ. Ned.-Ind. Publ. Hlth Serv.* **26**, 48.
— — (1938) *Z. Vitaminforsch.* **7**, 1.
Menken, J. G. (1932) *Dtsch. med. Wschr.* **58**, 1484.
— (1934) Thesis Utrecht.
Meulemans, O., and de Haas, J. H. (1936) *Indian J. Pediat.* **3**, 57, 133.
Wolff, L. K. (1936) *Schweiz. med. Wschr.* **66**, 979.

MEDICAL TOUR TO THE U.S.S.R.—The Society for Cultural Relations with the U.S.S.R. is again arranging for a medical party to visit Russia. Opportunities will be given for studying aspects of medicine in which members of the party are specially interested, and Soviet hospitals and medical institutions will be inspected. In order to avoid the holiday season in Russia the party will leave London by sea for Leningrad on Sept. 7th, returning to Hull on Oct. 2nd. The itinerary will include Moscow, Kharkov, and Kiev. Further information may be had from the secretary of the society, 98, Gower-street, London, W.C.1.

MEDICAL SOCIETIES

ROYAL SOCIETY OF MEDICINE

SECTION OF SURGERY

AT a meeting of this section on May 4th Prof. G. GREY TURNER delivered his presidential address on

Non-malignant Stenosis of the Œsophagus

He said that his special interest in non-malignant stenosis of the œsophagus dated back to an occasion in Newcastle-on-Tyne when autopsy disclosed a wonderful example of fibrous stricture of the œsophagus where malignant disease had been confidently expected. He had always been taught that cancer of the œsophagus was almost the only cause of œsophageal obstruction, but he had been struck by a casual remark made by W. J. Mayo in 1906 that it was always worth while doing gastrostomy because the diagnosis might be wrong! The student who searched the museums would not find very many specimens of simple stenosis, but there was one beautiful example at Bart.'s and a very striking one in the museum of the Royal College of Surgeons of Edinburgh. During the last few years the president had seen many examples of the condition. One that particularly impressed him was in an old woman admitted to hospital as a case of cancer. She was miserably thin, ill, and starved, and on the radiological evidence gastrostomy was carried out. Improvement was so remarkable that further investigations were made, disclosing only a fibrous stricture. Unhappily this patient died; at autopsy the innocence of the stricture was confirmed. Some of these cases were difficult to manage but responded well to treatment. A child, aged 3, in 1910, for example, whom he saw under the care of Rutherford Morison, was so voracious that he was constantly eating and regurgitating whatever was put before him; the stricture was dilated through the œsophagoscope and later by bougies, which he learned to pass himself, and twenty-five years later he was still well and with full swallowing capacity. For years now it had been assumed that strictures could be successfully dilated and perhaps cured under the guidance of the eye through the œsophagoscope, but this was not always successful and was often risky. Perseverance with bougies by the mouth was a safer if slower method which had cured several patients who had defeated the experts with the œsophagoscope. The president recalled a successful case of a woman whose stricture was overcome at first by the retrograde passage of bougies, followed by a rubber tube, the patient being taught later to pass bougies by the mouth. Another method sometimes applicable was cardioplasty following exposure of the œsophagus from the abdomen. The method of anastomosis between the œsophagus and the cardiac end of the stomach was not often indicated, but he had employed it in seven cases with very good results.

The *cause* of fibrous stricture was usually obvious, most cases resulting from the swallowing of corrosive fluids. Other causes could be local or general infections or acute fevers. Mild destructive changes in the œsophagus, the result of regurgitation of very acid or perhaps toxic stomach contents in patients who had lain extremely ill, might occasionally lead to stenosis. Brown Kelly of Glasgow had brought forward convincing evidence that a secondary fibrosing condition might start in association with some mild congenital defect. This was the only explanation in some cases which fitted with the facts.

Diagnosis not of the cause but of the actual condition was usually obvious, but sometimes presented difficulties, patients being treated for apparently innocent stricture which afterwards proved to be malignant.

The *prevention* of stenosis in the presence of such conditions as are almost invariably followed by its development was an important aspect of the question. One school of thought associated with the name of H. Salzer advised the passage of instruments in the very early days, although traditional teaching was in favour of deferring any such treatment until four or six weeks after the accident. The president had seen a perforation of the œsophagus from the bougie on the twenty-sixth day after the swallowing of carbolic acid, and he said he would hesitate very much to use any such dilatation until the stage at which fibrosis had become well developed. The recollection of Prof. John Chiene's dictum, "once a stricture, always a stricture," reminded him to comment on the ultimate condition of patients who had suffered from cicatricial stenosis of the œsophagus. Many of them, possibly the majority, might be permanently cured by persistent treatment, but there was probably a residue of cases in which the tendency to recurrence persisted for many years and possibly throughout life. One of his patients, who first showed signs of such a lesion at the age of three, had been treated with great success, and now at sixteen was able to swallow normal food like the rest of the family; but having of late years neglected the regular use of the bougie, she now got some pain behind the sternum and a radiogram showed a hold-up at the lower end of the œsophagus. Trousseau, the French clinician, had said that a patient using œsophageal bougies would die of the instrument sooner or later, and certainly there was danger in this treatment. The president had not himself witnessed a disaster in his own cases and his experience led him to conclude that the careful self-passage of bougies, blind though it may be, was no more dangerous than more rapid dilatation through the œsophagoscope.

But there were other methods available. The swallowed string, usually associated with the name of Plummer, should be tried in difficult cases before more drastic measures were adopted, though it was sometimes either useless or badly tolerated. Successes had been reported from the retrograde passage of bougies through a gastrostomy. Rapid divulsion and cutting through the stricture with a string saw were both violations of surgical principles. Attempts at excision of a simple stricture with end-to-end anastomosis was impracticable. In cases that had defeated the various methods mentioned there was always the possibility of short-circuiting the disability by making a new œsophagus, and to this end a vast amount of ingenuity had been exercised. The records of the numerous cases in which this plan has been tried suggested, however, that other and simpler means might often have prevailed. A colleague visiting Russia had seen no less than eleven patients in one hospital in Moscow all suffering from simple stricture of the œsophagus, the result of swallowing caustic fluids in suicidal attempts, and all being subjected by the surgeon in charge to treatment by formation of a new œsophagus. Such a wholesale resort to this measure could hardly have been necessary. It was clear that every effort should be made to restore Nature's path before attempting to replace it by a surgical exploit of such magnitude.

A MOCK TRIAL

FEATHER *v.* WATSON AT KING'S COLLEGE HOSPITAL

THE members of the Listerian Society, King's College Hospital, promoted a successful mock trial on May 4th. His Honour Judge EARENGEY, K.C., presided.

THE PLAINTIFF'S CASE

Mr. J. MAX MULLER, counsel for the plaintiff, Mrs. Feather, explained that she was 29 years old and living apart from her husband. She sued Dr. Watson for negligence on these facts: She consulted him on Jan. 15th, 1937, complaining of tiredness, nervousness, and palpitation. He diagnosed nervous depression and advised her to go on a sea voyage to the Mediterranean. On Jan. 30th she sailed. The Channel and the Bay of Biscay were very rough, both on the outward and on the return journey. The Mediterranean was infested with Spanish warships, which made her very anxious and spoilt any chance of recuperation. On the return voyage she was thrown down by the rolling of the ship and hurt her head. On her return to England she consulted a specialist named Dr. T. S. F. West, who found that she was suffering from severe exophthalmic goitre. He took her at once into a nursing-home and called in Mr. Hunter, who operated on Feb. 27th. She made an uninterrupted recovery. She now sued Dr. Watson for negligence in failing to diagnose her condition correctly and in treating her in a manner which caused her loss and suffering. She claimed 30 guineas for the cost of the unnecessary cruise, 100 guineas for the operation, 64 guineas for nursing-home fees, and 10 guineas for Dr. West's fee.

Mrs. Feather said in evidence that she had always been highly strung. Her eyes were not prominent before 1937. She had become more nervous since separating from her husband, and had lost weight. She had complained to Dr. Watson of tiredness and of being run down and nervous, with palpitations. She had been much worse by the time she had got to the Mediterranean and had spent most of the time in bed. She had left the ship in a stretcher and had been in bed for a fortnight in the care of Dr. Watson, who had seemed very casual.

In *cross-examination*, she agreed that she had been married at 23 and separated at 25, and had been anxiously hoping for a reconciliation with her husband, which had, in fact, taken place since the operation. She had been losing weight for 18 months. She had talked to Dr. Watson very fully about her matrimonial troubles. At that time she had had no swelling in the eyes or throat. He had told her not to worry and that she wanted a rest, and they had discussed the matter.

In reply to his Lordship, she agreed that she had felt very nervous on account of the Spanish troubles in the Mediterranean but had not thought of them before starting, her geography not being very good. She agreed that she studied her appearance from time to time in the mirror, and that up to Jan. 3rd she had not noticed anything wrong with her throat or eyes. She had thought that her heart was wrong.

Dr. Alister Maclagan, surgeon on s.s. *Empress of Abyssinia*, said in evidence that he had seen Mrs. Feather on the second day out, when she was very sea-sick. He had noticed a very rapid pulse and slight exophthalmos and had supposed that she was a known exophthalmic patient sent for a voyage before operation, and was surprised that her general practitioner had not written to him. He had done his best to keep her in bed, but she had got up and done more than he would have advised. The roughness of the sea made her very ill, and fright in the Mediterranean contributed. He had told her she was suffering from thyrotoxicosis.

Cross-examined, he maintained that her condition was getting worse, while her disease was steadily maintained throughout the voyage. By that he meant that mentally she was worse and physically the same. He agreed that the first day out on the cruise was an interesting day but would not admit that it was an unpleasant one. The sea had been "fairly rough" but not "rough." In the presence of brisk reflexes and tachycardia he would expect thyrotoxicosis. He agreed with the Judge that separation from her husband and anxiety about it would tend to the development of this trouble.

Dr. T. S. F. West said that Mrs. Feather had told him she had no general practitioner but came on Dr. Maclagan's recommendation. She was obviously suffering from severe Graves's disease, with slight exophthalmos, wasting, tremor, some enlargement of the thyroid, pulse 130, and blood pressure 145/75. She needed operation at once, and he had arranged for it. She must have had Graves's disease when Dr. Watson had seen her. This condition was difficult to diagnose but the possibility should be borne in mind. He would have expected a doctor at least to take the blood pressure, and to see whether a rapid pulse was transient or permanent.

Cross-examined, he agreed that he had seen Mrs. Feather for the first time six weeks after Dr. Watson had seen her. Tachycardia, brisk reflexes, and the general picture were enough to arouse suspicion of thyrotoxicosis. He admitted that there were other causes of tachycardia, such as alcohol, tea, and physical exertion, and that all neurotic patients were not inevitably hyperthyroidic. He admitted that a general practitioner must go very slowly in these matters.

Mr. M. C. Hunter, the surgeon, said that Mrs. Feather had shown obvious signs of exophthalmic goitre, though the eye appearance was not severe. He had found her basal metabolic rate to be +55 per cent. He thought she had had the disease in January but that the voyage had probably made it worse.

Cross-examined, he said that if he had not operated he would have put the patient to bed and tried the effect of iodides and medical treatment. He accepted what Dr. Watson had found but regarded it as incomplete. Blood-pressure reading should have been taken. The taking of a blood pressure was not deleterious to health. The doctor who was assessing his patient's condition with a view to sending her abroad ought to be sure of his diagnosis first.

Mrs. Feather was recalled on the quantum of damages, and this concluded her case.

THE DEFENCE

Mr. DAVID KARMEL, counsel for Dr. Watson, said in opening the defence that the plaintiff must prove that she had suffered from hyperthyroidism on Jan. 15th, that she had suffered damage because she had not been operated on until Feb. 23rd, and that Dr. Watson had been negligent in not diagnosing Graves's disease on Jan. 15th. The degree of skill required by law from Dr. Watson was only the reasonable degree of care and skill that a prudent person would exercise when examining a patient. It was not as high a degree as would be expected of a specialist. Dr. Watson could not be expected to diagnose an unusual disease like hyperthyroidism. He

had had a nervous patient, had very reasonably thought that she was suffering from a degree of neurasthenia, and had prescribed a perfectly proper treatment.

Dr. Watson said in evidence that Mrs. Feather was a very neurotic woman with a neurotic past history and had ample cause for her present state in her matrimonial troubles. He had found her nervous with very brisk reflexes, and very voluble. She had had no exophthalmos but a little tachycardia; she had been excited. There had been no obvious thyroid enlargement. He did not think she had hyperthyroidism then. He had thought of it as a possibility but had not felt justified in putting her to the expense of investigation. He had not taken her blood pressure, and said that even insurance companies did not ask for the blood pressure of applicants under fifty-five. He thought that the hyperthyroidism had been brought on by fright over the Spanish warships. He had intended to treat it, but had considered that she first needed rest. He had said nothing to her about consultation or investigation, because there had been no use in worrying her. She had gone to Dr. West without his knowledge.

Cross-examined, he said that he had seen thyrotoxicosis before but had seen a greater number of cases of neurasthenia. All the symptoms of nervous depression appeared also in Graves's disease. A Mediterranean trip would not harm a Graves's patient. No steps that he could have taken would have satisfied him that she had Graves's disease.

Re-examined, he said that she had no dilatation of pupils or dampness of hands.

Mrs. Trotter, the stewardess who had attended to Mrs. Feather on the liner, said that she did not think Mrs. Feather was ill, although she was fussy and a perfect nuisance. She had been nervous about the Spanish warships, but none had ever appeared.

Sir Thomas Standstill, the greatest living expert on diseases of the thyroid, who gave his address as c/o Moss Bros. and said he also had a sofa in Harley-street, agreed that many symptoms were common to neurasthenia and thyrotoxicosis. He said that he had not seen Mrs. Feather during her illness. This type of case was very difficult to diagnose, as the symptoms of simple neurasthenia and mild hyperthyroidism might appear identical. Dr. Watson's diagnosis of nervous debility might have been perfectly correct. A sea voyage would be admirable treatment for a mild case of Graves's disease, as a preliminary to an operation. The blood pressure would not necessarily tell a general practitioner whether a patient had Graves's disease. A reading such as had been given in evidence was not abnormal. The tests which had been mentioned were not necessarily diagnostic of Graves's disease. The symptoms Dr. Watson had found, coupled with those he had not found, were consistent with a negative diagnosis. A basic principle of treatment was to put the patient into fresh surroundings.

THE SUMMING-UP

The learned judge summed up strongly in favour of the doctor, but the jury, after a considerable absence, returned a verdict for Mrs. Feather with damages at 30 guineas, finding that the doctor had been negligent and that the patient had thereby taken an unnecessary cruise, but that none of her other loss had been due to his negligence.

The audience, on appeal, found by a large majority for the doctor.

Replying to a general vote of thanks, Judge Earengey said that the trial, besides being carried out admirably, must have served a valuable purpose in showing junior medical men the way in which courts did their work. It would help them to overcome the dislike which most doctors felt at first for the legal system which occasionally drew them into the courts as witnesses and subjected them to what they might consider as a certain amount of pulling-about in cross-examination. When they came to the courts as parties they had much stronger grounds for anxiety, because no one could tell what a jury would do. He strongly recommended every practitioner to insure himself by membership of a defence society.

REVIEWS AND NOTICES OF BOOKS

A Textbook of the Practice of Medicine

Fifth edition. By Various Authors. Edited by FREDERICK W. PRICE, M.D., C.M., F.R.C.P., F.R.S. Edin., Consulting Physician to the Royal Northern Hospital; Senior Physician to the National Hospital for Diseases of the Heart. London: Humphrey Milford, Oxford University Press. 1937. Pp. 2038. 36*s*. (India paper, 45*s*.).

FEW can appreciate the rapidity of the advance of medicine better than the conscientious editors and authors of text-books. The amount of rewriting and revising that four years have called for in Dr. Price's book is surprising; it involves not merely the addition of new information but alterations in presentation, the discarding of views and practices no longer current, and a shifting in many places of the emphasis and the perspective. It is to the credit of Dr. Price and his collaborators, most of them senior men, that so much of this has been done. Five of the contributors to the fourth edition have been removed by death. Their successors are Dr. Maurice Campbell, who revises the section on diseases of the blood-vessels; Dr. A. E. Gow, who collaborates with Lord Horder; Prof. J. W. McNee, who writes a new section on diseases of the spleen and the reticulo-endothelial system; Dr. F. M. R. Walshe, who revises the neurological articles; and Prof. Mapother and Dr. Aubrey Lewis, who conclude the book with an excellent short presentation of psychological medicine. Two thousand pages make a bulky volume; so the publishers this time offer an alternative edition on India paper, which is delightful to handle though it needs to be read in a very good light. "Price," in London at least, is probably the students' favourite among the larger text-books of medicine. This edition bids fair to maintain its prestige, and to fulfil its editor's wish that it should be considered "not unworthy of English medicine."

Handbook of Practical Bacteriology

A Guide to Bacteriological Laboratory Work. Fifth edition. By T. J. MACKIE, M.D., D.P.H., Professor of Bacteriology, University of Edinburgh; and J. E. MCCARTNEY, M.D., D.Sc., Director of Research and Pathological Services, London County Council. Edinburgh: E. and S. Livingstone. 1938. Pp. 586. 12*s*. 6*d*.

THE continued popularity of this handbook is easy to understand. A great deal of accurate information is compressed into a volume of small size. The subject is presented, as an experimental science should be, from the practical standpoint. The

technical methods given are good ones and are so clearly described that beginners will have no difficulty in getting the desired results if they follow the instructions with care. But over and above its use as a guide to sound technique this book provides an excellent general introduction to the study of bacteriology. Supplemented by the usual teaching of a medical school it should give the ordinary medical student all he needs and one who intends to specialise a sound basis for further work. The new edition has been thoroughly revised and the newer work on such subjects as the streptococci, food-poisoning, and the filtrable viruses is presented with judgment. There is in fact everything to praise and nothing to criticise in this excellent little book. Our only hope is that in future editions the authors will resist any temptation to enlarge it.

The Practice of Refraction

Third edition. By Sir STEWART DUKE-ELDER, M.D., Ch.B., F.R.C.S., Surgeon-Oculist to H.M. The King; Ophthalmic Surgeon and Lecturer in Ophthalmology, St. George's Hospital. London: J. and A. Churchill. 1938. Pp. 371. 12*s.* 6*d.*

THIS book has retained its practical and clinical character. It sets out the essential principles of the theory and practice of refraction and the correction of defects in the optical system of the eyes and their associated muscles. Descriptions of mathematical proofs have been omitted deliberately. The new matter in this edition includes a broad outline of such problems as aniseikonia, orthoptic exercises, dynamic retinoscopy, muscle imbalance, and contact glasses. For technical details the reader is referred to special monographs. It is good to see the emphasis laid on the assiduous and painstaking practice required before efficiency in refraction work can be achieved. This book provides a lucid and readable guide for the beginner.

Treatment in General Practice

Third edition. By HARRY BECKMAN, M.D., Professor of Pharmacology at Marquette University School of Medicine, Milwaukee, Wisconsin. London: W. B. Saunders Company. 1938. Pp. 787. 42*s.*

THIS book shares a fault common to many books on therapeutics written by specialists for general practitioners. The descriptions are not detailed enough. The author assumes that the practitioner should try something simple and, if it fails, should refer the case forthwith to a consultant, quite forgetting that if (as sometimes happens) the consultant fails, the burden of treatment falls once more upon the practitioner, whose knowledge of therapeutics should therefore be, and often is, extensive and peculiar. This edition, though it includes much new material, is no more bulky than its predecessors, whence the author congratulates himself on having learnt to be brief. When, however, reference to collapse therapy in tuberculosis is limited to six lines, some may think that brevity ceases to be a virtue. Prof. Beckman is needlessly sceptical about the value of endocrine extracts other than thyroid in the treatment of amenorrhœa, and only lukewarm about cortical extract for Addison's disease; he makes no reference to the comfort to be derived from valerian or to the uses of anterior pituitary and œstrin in the disorders of the menopause. Nevertheless an immense field of therapeutics is covered or at least touched upon in this edition and there are plenty of valuable suggestions; among them we noticed specially the notes on methods of treating burns, on the use of trichlorethylene in tic douloureux, and of pituitary extract in post-herpetic neuralgia. Except for the pernicious vomiting of pregnancy and eclampsia obstetrical matters have been deliberately omitted and so has the treatment of drug-addiction and of certain tropical diseases. Especially commendable from the practitioner's point of view is the chapter on the anæmias which are classified according to their therapeutic response.

Essentials of Psychiatry

Third edition. By GEORGE W. HENRY, Associate Professor of Psychiatry, Cornell University College, New York. Baltimore: Williams and Wilkins; London: Baillière, Tindall and Cox. 1938. Pp. 465. 22*s.* 6*d.*

Manual of Psychiatry and Mental Hygiene

Seventh edition. By AARON J. ROSANOFF, Los Angeles, California. London: Chapman and Hall. 1938. Pp. 1091. 37*s.* 6*d.*

Principles and Practice of Clinical Psychiatry

By MORRIS BRAUDE, M.D., Associate Clinical Professor of Psychiatry, Rush Medical College, University of Chicago. Philadelphia: Blakiston's Son and Co. 1937. Pp. 382. 18*s.*

THESE three text-books indicate the importance attributed to dynamic psychological interpretations in American psychiatry, and the bareness of the knowledge upon which such interpretations still rest in the United States as elsewhere. The psychobiological passages in the works by Dr. Henry and Dr. Rosanoff are sensible and useful as far as they go. But they seem stale, vague, and a trifle perfunctory in comparison with the detailed information, including the fruits of much research reported since their last editions, which they are able to give in the other pages of their books. It is not that the authors are half-hearted in advocating and presenting this aspect of psychiatry, but that they cannot, except by invoking Freudian psycho-analysis, find anything precise or novel to say; they are, it is true, benevolent towards psycho-analysis, but with the qualified benevolence of a fair-weather patron. No one, however, who had read these or other modern text-books could have any excuse for continuing to talk of the "descriptive psychiatry" of the "alienist." Dr. Henry's new edition is considerably enlarged, and is an admirable, reasonably comprehensive, conventional presentation of the subject. The references given in the text—mainly to American articles—are numerous and well selected, and there is a list of relevant books in the English language which shows what an unmanageably wide field the psychiatrist has to cover: he is lucky if he escapes sciolism.

Dr. Rosanoff's book is of a more ambitious kind. Himself an active research worker, he seems to have had readers with similar interests in mind, and the outcome has been a well-documented, learned, but not very well-proportioned survey of the present position. With an unusually wide, though erratic, grasp of the literature, especially on those topics which he has himself studied, and a strong bias towards an ætiological classification based on organic pathology, he is evidently now unable to produce as easy and consecutive an account of the whole subject as he supplied in his earlier editions; most of the book has been rewritten. Dr. Rosanoff's method of presentation is peculiar and at times eccentric; his

attempt to split up schizophrenia into psychoses of traumatic, infectious, and other organic and toxic ætiology, leaving a residue to be dealt with under the heading of chaotic sexuality, is at best premature, and in its present form decidedly unsuccessful. The book is swollen with two hundred pages of information about psychological and other diagnostic procedures, and by more than a hundred case-records. This work, with its strongly individual point of view, is now less suitable for the medical student than for the graduate.

Dr. Braude's book is on a different level from the other two. It puts the essentials of the subject simply, evades problems that might perplex the beginner, and is enlivened by illustrations from history and literature. It would be a queer student who could make against the psychiatry here presented that common complaint "It's all above my head." The work is however too superficial and easy-going to be worthy of its imposing title, though its chapters might serve as the basis of clinical lectures designed to hold the attention of students while giving them a rough knowledge of the subject. The style is wordy, and the bibliographies given at the end of each chapter are almost satirical comment on the custom of sending students to the original sources. The references, mostly limited to publications of the last seven years, are drawn from an amazing miscellany of journals; there are no less than sixteen references appended to a chapter containing only seven pages, and of these sixteen papers one is in Russian, one in Japanese, and another in Spanish. A bibliography in a text-book designed for students should surely be selected from works that are likely to be accessible to him and limited to key articles. If he wants to pursue a subject he will find therein pointers in the right direction.

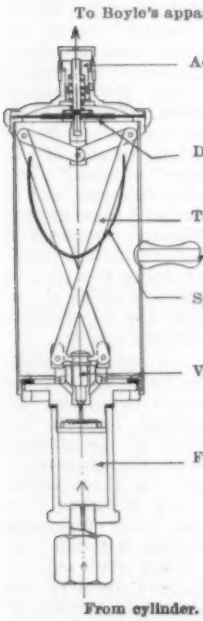
NEW INVENTIONS

A LOW-PRESSURE REDUCING CHAMBER FOR ANÆSTHESIA

Boyle's apparatus has become the standard British machine for the administration of nitrous oxide, oxygen, and ether in this country and because of its simplicity it is likely to remain so. There are better machines but they are generally too expensive for use by the general practitioner.

I have had certain alterations made to a Boyle's apparatus that I think improve the machine. I use the Evans type of stand to hold gas-and-oxygen cylinders, with a small fitting on the side to hold a carbon dioxide "Sparklet." The principal change in the machine is a new type of reducing valve that works at a very low pressure. There are two of these reducing valves, one for oxygen and one for nitrous oxide, and they are fitted to a coupling that joins two gas and two oxygen cylinders.

The reducing valve consists of a chamber for reducing the pressure, which is done by a system of toggle-links and a valve, as shown in the Figure.



THE REDUCING CHAMBER.

On opening the cylinder valve the gas passes through a filter chamber to ensure that no foreign matter enters the reducing chamber. With the adjusting nut slackened off, the gas will not pass the valve, which is operated by a pair of toggle-links kept in tension by a spring, the toggle-links being connected to a diaphragm. By screwing down the adjusting nut on to the diaphragm, the toggle-links lift the valve and allow the required amount of gas to pass into the chamber and out through the nozzle to the rubber tube and thus to Boyle's bottles. The apparatus is made by the Dental Manufacturing Company, London, W.1.

The great advantages of the very low-pressure reducing valve is that when the machine is being used for endotracheal work it is impossible to give too high a pressure of gas or oxygen. The pressure at which the gases are running is so low that, by shutting off the rebreathing bag, an increased flow of gas is sucked in by the patient.

If it is desirable to give a sudden extra supply of oxygen to the patient, all that need be done is to shut off the rebreathing bag, turn off the nitrous oxide, and the negative pressure on inspiration will immediately and automatically enable a large dose of oxygen to be inhaled. For example, oxygen is flowing through two holes in the mixing bottle and the rebreathing is shut off; when the patient inspires, oxygen will flow through all the holes and out of the extra outlet of the tube as well. The pressure can be varied within limits by turning a screw at the top of each reducing valve. When the anæsthetist wishes to give a full flow of gas he simply opens the by-pass on the Boyle's bottle and the resistance of the water in the bottle being removed, there is an immediate full flow of gas without any change of the adjusting screw.

I have not used flow meters in my machine because of their expense and I think that the average general practitioner anæsthetist will feel the same about these, excellent though they may be.

To the metal part of the rebreathing bag I have attached a small inlet tube that just fits the outlet tube of an ethyl chloride container, so that if one desires to give ethyl chloride in the induction period, this can be sprayed into the bag as desired.

The nitrous oxide low-pressure reducing chamber can be used for the administration of nitrous oxide and air in midwifery by using some intermittent-flow device, such as the D.M.C. carburettor. Low-pressure gauges may be fitted to the reducing chamber, and the nitrous oxide chamber should always have one of these gauges if it is to be used for the administration of analgesia in labour.

High-pressure gauges are attached to the couplings joining the gas-and-oxygen cylinders to enable the anæsthetist to know approximately how much they contain.

J. E. ELAM, M.R.C.S. Eng.
Consulting Anæsthetist to the British Hospital for Mothers and Babies, Woolwich.
New Barnet.

THE LANCET

LONDON: SATURDAY, MAY 14, 1938

DOCTORS AND THE HERBERT ACT

THERE are precedents which encourage the belief that Parliament cannot always think of everything. Some of them indicate that the matters likely to be overlooked are those which concern the medical profession. Whether the community intends it as a compliment or not, doctors are generally taken for granted. Last July the Matrimonial Causes Act, associated with the name of Mr. A. P. HERBERT, M.P., gave husbands and wives the right to petition for divorce on the joint grounds of incurable insanity plus five years' detention in a mental hospital. The degree of the patient's curability is a fact which can scarcely be established without medical testimony. Any approach to the topic of lunacy certification inevitably recalls to the medical practitioner the shock of such verdicts as were given in Harnett *v.* Bond and similar cases. Once bitten, twice shy. It may be that the doctor's testimony under the relevant provision of the Herbert Act will be immune because all evidence given in a court of law is absolutely privileged. If there be any doubt about this, doctors may fairly demand its elucidation. But that is not the end of the matter. The practitioner still owes the patient the duty of non-disclosure. Thus once again there emerges the hackneyed question "Should a doctor tell?"

The five-year period of detention, one of the two points to be established by a petitioner, should be susceptible of easy proof. Yet even here there lurks a difficulty. The period, as defined in the Act, may include any period of voluntary treatment under the Mental Treatment Act of 1930, provided that the voluntary period follows immediately upon the conclusion of a period of detention on order or inquisition. If the patient has been released from detention and transferred to voluntary treatment, the fact may well suggest to the judicial mind that the mental illness is showing signs of improvement. In such a case there may be almost a presumption against incurability. What will be the effect upon the other point to be proved by the petitioner—namely, that the respondent is "incurably of unsound mind"? Here the judges, accustomed to sift evidence and to arrive at conclusions of fact, will no doubt face the question without undue fear. The medical witness will express his opinions and expound the reasoning and experience on which they are founded; those opinions will by no means be final. The judge will listen and allow such weight as he deems fit, applying a legal rather than a medical standard of insanity; he himself will decide the issue of curability. Expert views will doubtless vary. Some will deem recovery after five years as highly improbable; others will be more optimistic. At a recent meeting of the Medico-Legal Society Mr. Justice TRAVERS HUMPHREYS observed that the occasional miracle might occur in any type of case. "All that any court or doctor can do is to say, 'Taking into consideration all the well-known facts of the case, we think it so unlikely that this person will ever be cured for the purpose of leading a reasonable married life that we will regard him as incurable in the sense of the Act.'" If this be the official view, it is a helpful indication.

There remains, however, the dilemma of professional secrecy. The new law, as Mr. LATEY reminded the Medico-Legal Society, permits a mental patient to have a decree of divorce pronounced against him without his even knowing that a petition has been filed. If at the end of the five-year period the patient is undergoing voluntary treatment and not detention, will he not be entitled to full information of what is afoot? Voluntary treatment is a compromise and an anomaly; the patient can take his discharge and walk out of the hospital in which he voluntarily resides. If so, do not the medical practitioners who treat him owe him the duty of secrecy? Normally, as Dr. RICHARD DURAND wrote lately in our columns, they would probably not hesitate to discuss the health and prospects of a husband with a wife or vice versa. But, if husband and wife are on opposite sides in litigation, has not the practitioner an obligation to refuse his evidence on the grounds of professional confidence? Parliament ought to offer some solution of these problems which it creates. Last Monday, during discussion of another Bill for the general amendment of legal procedure, Mr. HERBERT formally expressed regret that the Bill omitted to alter his own recent Act so as to clear up this and other difficulties which were already defeating its good intentions. Perhaps he will pursue this point further at a subsequent stage. The ideal solution may well be that of those critics who say that our whole system of lunacy certification should be overhauled and that the duty of certifying should be entrusted to panels of official examiners. The Matrimonial Causes Rules at present prescribe that, in proceedings for nullity on the ground of impotence or incapacity, the petitioner must apply for the appointment of medical inspectors to examine the parties. Cannot this arrangement be extended to obtain the independent opinion of experts upon the question of curability?

WAYS OF GIVING SEX HORMONES

WHETHER an endocrine preparation is effective by mouth seems to depend on its chemical complexity. The active principle of the thyroid, which is probably a tripeptide containing the amino-acids thyroxine and diiodotyrosine, is a comparatively simple compound and can be absorbed through the mucous membrane of the small gut so freely that parenteral injection is unnecessary.

Theoretically the sex hormones, which are sterols, should also be absorbable from the alimentary tract, and this is certainly true of the œstrogens, for œstrin by mouth often yields spectacular results in the menopausal syndrome. Œstriol is absorbed in larger proportion than œstrone when given by this route, though it is less potent when injected; but either of these forms is suitable for oral use, provided one bears in mind that the dose must be (according to various estimates) between five and thirty times as high as the dose for injection. Progesterone and the androgens, being sterols, should also be absorbed from the intestine; but the technical difficulty of obtaining high enough concentrations prevents their being given in this way. At the moment there is no convincing evidence that any other hormone is effective by mouth, and the oral administration of polyglandular mixtures is likely to be correspondingly valueless. This is true of anterior-pituitary preparations as well as others; for the confidence of some clinicians in their efficacy is not borne out by animal experiment.

In the treatment of diabetes insipidus, posterior-pituitary extract is often prescribed in the form of snuff, and some of the unpleasant symptoms arising from infrequent injection of large doses may thus be avoided by frequent inhalation of small ones. It was hoped that anterior-lobe hormones likewise might be absorbed from mucous membranes, but gonadotropic extracts have in practice proved ineffective when placed in the vagina. Œstrogens, on the other hand, can certainly be given in this way, and vaginal suppositories are sometimes employed in the treatment of local vaginal lesions associated with ovarian deficiency. On another page of this issue Prof. BERNHARD ZONDEK writes on the application of hormones to the skin, which in the case of the œstrogens may be preferable to ingestion, since it allows of more complete absorption, especially (he finds) when an alcoholic tincture is used. Such a tincture is an improvement on the œstrogenic ointments previously devised by ZONDEK which have been used chiefly in cases of subnormal mammary development, being applied locally to the breasts. Mammary tissue appears to be specially sensitive to this form of œstrogenic stimulation; indeed males employed in packing ampoules of œstrogenic material are apt to develop tender swelling of the breast from the continual handling of the œstrogenic compounds. The success of percutaneous administration has even led to the inclusion of œstrogens in cosmetic creams, but "hormone face creams" enjoy an undeserved popularity when they claim to have specific properties as skin foods. Their promiscuous distribution is, moreover, not without danger, for if they have an appreciable content of œstrogen and are applied continuously as recommended they may derange the menstrual cycle, if they do nothing worse.[1]

To get satisfactory results from endocrine preparations, then, most of them have to be given by injection, and the sterol hormones, which are soluble in high concentration only in oil, have to be injected intramuscularly. This introduces the problem of how to prolong the action of single doses so as to avoid frequent injections. It has been found that the duration of effect is directly proportional to the insolubility of the compound in the body fluids, and this principle underlies the use of the new insulin compounds, such as zinc protamine insulin. In endeavouring to reduce the solubility of the sex hormones it has been discovered that their administration in the form of an ester, such as œstradiol benzoate or testosterone propionate, considerably lengthens the period of action, so that a constant level of effect may be obtained by twice-weekly injections of the former and weekly injections of the latter. Progesterone is more difficult to esterify, and at present no progesterone ester is available for clinical use, though progress is being made in this direction and reports have appeared of a progesterone ester that is effective by mouth. A method of obtaining a far more prolonged action has, however, been invented by DEANESLY and PARKES [2]—namely, the subcutaneous implantation of a tablet of compressed crystals of the pure hormone, from the surface of which the active principle is absorbed continuously in small quantities. This method is now being tested clinically, and its use in controlling the menopausal symptoms of a young female castrate has been described by BISHOP,[3] who found that a 14 mg. tablet of crystalline œstrone appeared to be effective for four or five weeks. Experiments are in progress to determine the most suitable shape and weight for the tablets.

[1] See *J. Amer. med. Ass.* April 9th, 1938, p. 1194.

THE PREMATURE INFANT

THE announcement in our last issue that the Royal College of Physicians of London has approved a "standard" of prematurity, based upon the birth-weight of 5½ lb. or less, represents a stage in an effort to improve the chances of the premature infant. During recent years the death-rate in the first month of life has not been reduced in anything like the same proportion as the general infant mortality-rate, which covers the first year. Roughly speaking about half the deaths in the first month can be attributed to prematurity; but there are variations in different parts of the country, and even in the same institution, according to the standards used. The dangers of being born early were well brought out by CAPON [4] in an address at the Royal Society of Medicine two years ago, and HESS [5] says that in Chicago nearly 60 per cent. of infants dying under thirty days of age are described as premature. It is generally felt among pædiatricians, and especially those associated with maternity hospitals and units, that more could be done for this group of infants;

[2] Deanesly, R., and Parkes, A. S., *Proc. roy. Soc.* B, 1937, **124**, 279; see also *Lancet*, 1937, **I**, 1354.
[3] Bishop, P. M. F., *Brit. med. J.* April 30th, 1938, p. 939.
[4] Capon, N. B., *Proc. R. Soc. Med.* 1936, **29**, 1189.
[5] Hess, J. H., *J. Amer. med. Ass.* 1936, **107**, 400.

and it is clearly worth doing, for if they can be steered over the early weeks of life the large majority grow into healthy boys and girls.

An attempt to tackle the problem has been made in recent years in Chicago with good results,[5] and an essential feature of the scheme there has been prompt notification of all premature births to the health authorities. If such a plan is to succeed it is evident that some sort of standard is necessary, and while experts can all describe what they mean by a premature baby they become somewhat vague when asked to frame an easy "definition." Questions to a public authority administering a large area with twenty-two maternity units showed that, in the returns in which premature babies were listed, eleven hospitals used no standard, four used weight alone (varying between 5 lb., 5¼ lb., and 5–5½ lb.), six used weight plus other considerations, and one used a length standard only (less than 18 in.). Strictly speaking, "prematurity" must mean a baby born before the full period of gestation; but it is notorious that the menstrual history is often unreliable and what matters essentially is that an infant born at supposed full term or less is "immature." Clearly a full-term twin may be small enough to have many of the characteristics of a "premature" baby, and hence the weight standard probably gets nearest to a simple means of defining what is meant by "prematurity."

In seeking for guidance the various bodies concerned (the Royal College of Physicians, the British College of Obstetricians and Gynæcologists, the section for the study of disease in childhood of the Royal Society of Medicine, and the British Pædiatric Association) have naturally paid attention to standards in use in other countries. The classical work of YLPPÖ [6] has had great influence on the Continent and 2500 g. or less is very widely used in Europe, a figure to which the 5½ lb. standard is approximately equivalent. The children's bureau of the United States Department of Labor had the matter under consideration some years ago and has accepted the basis of a weight standard of 2500 g. (DUNHAM [7]). This is in accordance with resolutions passed three years ago by the American Academy of Pediatrics,[8] which included the following: "A premature infant is one who weighs 2500 g. or less at birth regardless of the period of gestation." The proposal emanating from the Royal College of Physicians says the same thing in possibly a more exact manner. The essential feature of all the discussions and proposals is the weight of 5½ lb., and it should be comparatively easy to induce health authorities and maternity institutions to adopt this. Having the uniform standard established, the next step will be to see where are the good and where the bad areas in the country for premature infants. What is done in the better areas can then be studied in the hope of its being applicable to the worse.

ANNOTATIONS

SALT AS A THERAPEUTIC AGENT

How many medical men, asked to select the ten most valuable drugs, would include common salt on their list? And yet it has an undoubted claim; indeed few would omit it once they had thought of it in this connexion. Of its many uses we may here mention two, one of which is new. In the United States Sandstead and Beams [1] claim that administration of sodium chloride in large doses (0·25 to 0·5 g. per kg. body-weight per day) leads to complete or almost complete relief of the pain of diabetic neuritis and to improvement in the peripheral circulation of elderly diabetics. If this claim should be substantiated, the physician with diabetics under his care will be provided with a much-needed remedy. In India Chakravarti and Tyagi,[2] under the title of "studies in effects of heat," describe 10 cases of collapse during the hot weather at Allahabad. In all 10 there were signs of severe salt deficiency and its attendant renal complications, and it is clear that these patients would probably not have collapsed if they had been taking enough salt with their food. These are glaring examples of serious deficiency disease. It is axiomatic that for one example of a frank deficiency disease there must be hundreds of other masked and subacute forms in the same district. The observation of Chakravarti and Tyagi therefore support the view already expressed in our columns,[3] that mild degrees of salt deficiency must be a common source of chronic ill health in the tropics.

[1] Sandstead, H. R., and Beams, A. J., *Arch. intern. Med.* March, 1938, p. 371.
[2] Chakravarti, D. N., and Tyagi, N., *Indian J. med. Res.* January, 1938, p. 791.
[3] McEwen, O. R., *Lancet*, 1935, **1**, 1015; McCance, R. A., *Ibid*, 1936, **1**, 767.

PROSTIGMIN AND INTESTINAL MOTILITY

PROSTIGMIN, investigated in 1931 by E. Stedman as a stimulant of the parasympathetic system, has been used by several observers to increase intestinal activity and in particular to relieve post-operative intestinal atony and distension. This synthetic compound resembles physostigmine in its action on the alimentary tract, but in therapeutic doses has little action upon the cardiovascular system or the eye. In 1934 Carmichael and others,[9] reporting to the therapeutics trials committee of the Medical Research Council, confirmed its freedom from side-actions on the circulation and eye in doses up to 0·0015 g. The drug increased the activity of the intestine, but the contractions and relaxations it induced had no propulsive quality, so that the evacuation of flatus or fæces usually required additional treatment in the form of enemata or pituitary extract. In the cases recorded the drug was given in one or two doses at wide intervals. Harger and Wilkey [10] now report their experience with prostigmin in 175 cases of post-operative distension or ileus and record excellent results in the prevention or treatment of these conditions; in their experience it gave relief in the majority of cases without any further assistance

[6] Ylppö, A., *Jb. Kinderheilk.* 1919, **24**, 1.
[7] Dunham, E. C., *J. Pediat.* 1936, **9**, 17.
[8] *J. Pediat.* 1936, **9**, 104.
[9] Carmichael, E. A., Fraser, F. R., McKelvey, D., and Wilkie, D. P. D., *Lancet*, 1934, **1**, 942.
[10] Harger, J. R., and Wilkey, J. L., *J. Amer. med. Ass.* April 9th, 1938, p. 1165.

from enemata and the like. The doses employed were similar to those used by Carmichael and his colleagues (namely, 1–2 c.cm. of 1/4000 prostigmin methyl sulphate); but they were repeated at intervals of 2–4 hours until improvement resulted, and as many as nine doses were employed on occasion without any unpleasant effect.

Prostigmin belongs to the group of drugs that inhibit the action of the enzyme choline-esterase present in the blood and tissue fluids. These anti-cholinesterases impede the destruction of any acetylcholine produced in, or introduced into, living organisms. The action of the parasympathetic system upon the intestinal movements is cholinergic —i.e., it is associated with the production of acetylcholine at the nerve-endings in the intestinal wall—and anything that tends to preserve the acetylcholine so formed may augment the peristaltic activity produced. In experimental work the augmentation of acetylcholine effects is usually obtained by continuous perfusion of the tissue with a solution containing an anti-cholinesterase. It appears possible that the greater efficacy of prostigmin in repeated doses, as employed by Harger and Wilkey, depends upon the maintenance of a more uniform state of acetylcholine preservation in the body than can be achieved with a single or widely spaced doses. If this interpretation of the action of prostigmin is correct, it offers a reasonable explanation of the different findings of Carmichael and of Harger and Wilkey, and indicates the therapeutic importance of repetitive dosage.

ATELECTASIS AFTER ANÆSTHESIA

A RECENT discussion[1] at the Royal Society of Medicine showed substantial agreement among physicians, surgeons, and anæsthetists that collapse of the lung is generally the result of obstruction to a bronchial tube. But several speakers then cited cases in which no such obstruction was present, especially when atelectasis followed rapidly on external injury to the thorax. The nature of the anæsthetic was felt to bear only indirectly on the production of atelectasis, the salient predisposing factors being the site of operation, its duration, and the condition of the patient before operation. O. M. Jones and E. E. Burford have now[2] described massive collapse following administration of Cyclopropane in which atelectasis was in their opinion due to absorption of gases in the alveoli. They point to the great variation in the rate of this absorption in relation to the gases present. Anæsthetic vapours, oxygen and carbon dioxide are all absorbed in minutes whereas the inert gases—nitrogen, helium, and hydrogen—require hours. Bearing this in mind, it is easy to see the possibility of massive collapse following cyclopropane inhalation without any bronchial plug. As the inhalation continues the bronchial atmosphere may become devoid of inert gas except for the small amount of nitrogen brought from the tissues to the lungs by the blood in simple solution and diffused into the alveoli. As the blood normally contains about 1 per cent. nitrogen the amount so brought would have little effect in alveoli accustomed to a nitrogen tension of 80 per cent. When the alveoli have lost the supporting properties of the inert gas conditions are present which favour atelectasis. The details of the four fatal instances in which the paper is based certainly give support to this theory. Jones and Burford recommend the routine use of helium during the administration of cyclopropane and describe the most convenient method of carrying this out. But, as we have already had occasion to point out,[3] helium is more readily obtainable for this purpose in America than here.

[1] *Lancet*, March 12th, pp. 613 and 619.
[2] *J. Amer. med. Ass.* April 2nd, p. 1092.

STUDIES ON TYPHOID FEVER ON THE WITWATERSRAND

IN a monograph issued from the South African Institute for Medical Research, Dr. W. Lewin[4] records a series of observations on the diagnosis, prophylaxis, and serum treatment of typhoid fever. He confirms the findings of A. Felix, and of many subsequent workers, in regard to the part played by the Vi antigen in determining mouse-virulence and immunising potency; and he notes, again in agreement with many other observers, that a vaccine prepared from a strain containing the Vi antigen will induce an active immunity in mice, even though the treatment employed in killing the bacilli has deprived them of the power of stimulating the production of Vi agglutinin in detectable amounts.

In a study of 229 strains of *Bact. typhosum* freshly isolated from cases of enteric fever, he finds, as others have done, that the great majority of such strains are of the form which Kauffmann has named V-W. These strains contain the Vi antigen, but not in so large an amount as to render the bacilli inagglutinable by an O antiserum in moderate dilution. Strains of Kauffmann's V type, in which the preponderance of Vi antigen inhibits agglutination in an O antiserum are relatively rare (18 of 229 strains), and strains of Kauffmann's W type, in which the Vi antigen is absent, or undetectable by direct agglutination, are rarer still (4 of 229 strains). No correlation could be observed between the severity of the disease and the type of infecting bacillus. The proportions of the different types in a small series of strains isolated from carriers were found to be very similar. It is noted that repeated examinations of a single carrier at considerable intervals of time may yield strains of all three types.

The sections on diagnosis deal in the main with an attempt to establish a "diagnostic titre" for H and O agglutinins, using standardised bacterial suspensions. Taking the obvious point of departure, though its obviousness has not always led to its adoption, the author first determined the frequency of agglutination at various titres among 442 samples of serum obtained from normal persons in the district concerned who gave no history of an attack of enteric fever, or of antityphoid inoculation. He found that 2·9 per cent. of these normal sera gave H agglutination at a titre of 1 : 100, while 2·0 per cent. gave O agglutination at 1 : 200. He adopted these titres for his diagnostic tests because (*a*) at this level the odds would be high against a false positive result, and (*b*) because most patients suffering from typhoid fever form agglutinin to titres as high or higher than these, so that there should not be many false negative results. Two series of cases are described in which this method was put to the test. Both series were observed in hospital. In the first series only one specimen of serum was examined from each patient. In 32 cases a provisional diagnosis of enteric fever on admission was confirmed by the isolation of *Bact. typhosum* from the blood or excreta. In 81 per

[3] *Lancet*, April 30th, p. 1008.
[4] Typhoid Fever on the Witwatersrand: Bacteriological Aspects, Serological Diagnosis, Specific Prophylaxis, and Specific Treatment. *Publ. S. Afr. Inst. med. Res.* 1938, **8**, 413–550.

cent. of these cases the agglutination reaction was recorded as positive. In 19 cases a provisional diagnosis of typhoid was confirmed on clinical grounds, but *Bact. typhosum* was not isolated. In 89 per cent. of these cases the agglutination test was positive. In 62 cases a provisional diagnosis of typhoid was not confirmed after observation in hospital. In 95 per cent. of these cases the agglutination test was negative. In a second series of cases, in which repeated tests were made on each patient, all of 34 cases from which *Bact. typhosum* was isolated and all of 15 cases of "clinically confirmed" typhoid, gave a positive agglutination test at some stage of the attack, while of 57 cases in which a provisional diagnosis of typhoid was rejected on clinical grounds, 96 per cent. gave only negative reactions.

The sections on prophylaxis deal mainly with a comparison between the results produced by subcutaneous inoculation of a vaccine ("typhoid endotoxoid") prepared by Grasset by the formolisation of frozen and thawed bacterial suspensions, and the administration of typhoid vaccine in large doses by mouth, as advocated by Besredka. The "typhoid endotoxin," like other bacterial vaccines, induces the formation of H and O agglutinins, but not of Vi agglutinins. The author's results with vaccination by mouth are in entire agreement with those of many workers who have reported a poor, or negligible, agglutinin response, following this procedure. The accounts of field trials suffer from the fact that in no case is it possible to compare the incidence of the disease in inoculated and control groups exposed to the same environment over the same period of time; but, so far as can be judged from a decreased attack-rate on a particular mine following mass immunisation, or comparisons between one mine and another, there is a strong suggestion that subcutaneous inoculation has a high protective value, while the administration of vaccine by mouth has very little.

In regard to serum therapy, a description is given of 62 serum-treated cases and 625 controls. In non-European patients the cases treated with serum showed a case-mortality of 23·8 per cent. as compared with 32·2 per cent. among the controls, while for European patients the corresponding figures were 7·3 per cent. as compared with 18·9 per cent. The serum employed in this series of tests contained no Vi antibody. A small series of more recent cases have been treated with a serum containing this antibody, with encouraging results; but no statistical assessment is yet possible. In a final section, a description is given of a small series of cases treated with increasing doses of a "typhoid endotoxoid" vaccine, apparently with beneficial results.

TESTOSTERONE IN GRAVES'S DISEASE

THE anterior lobe of the pituitary gland secretes a hormone that stimulates the thyroid. If Graves's disease is caused by excessive secretion of this thyrotropic hormone it might rationally be treated with hormones known to inhibit anterior-pituitary function.[1] On this basis Spence[2] in 1935 and 1936 gave œstrin to six women with toxic goitre, for periods up to three weeks; but it did them little or no good. In our correspondence columns this week Dr. Loeser records a similar attempt, using testosterone propionate instead of œstrin, and it will be seen that he is favourably impressed. His "first success" has however been anticipated; for Dr. Levy Simpson[3] has just recorded three other cases similarly treated, one of them since last October. All three patients felt and seemed the better for their treatment, and they took no harm from it. One of them had a toxic adenoma, and showed improvement in the electrocardiogram though not much otherwise. The other two, with Graves's disease, each gained about a stone within three weeks, and Simpson thinks it possible that "started early, or continued for a long period, testosterone propionate might prove to have a fundamental influence on the course of exophthalmic goitre." He adds, however, that the "anabolic" effect may be non-specific and partly due to water-retention.

[1] See *Lancet*, 1936, **2**, 990.
[2] Spence, A. W., *Ibid*, p. 970.
[3] Simpson, S. L., *Postgrad. med. J.* May, 1938, p. 144.

HOSPITAL REPORTS

THE scientific as opposed to administrative reports which an increasing number of London and provincial hospitals now publish annually or at more frequent intervals are of distinct types. The well-known *Guy's Hospital Reports*, for instance, published quarterly, contain only records of research in progress at the hospital which have not appeared elsewhere, whereas at the other extreme the *Collected Papers of the Middlesex Hospital Medical School* is a volume of bound reprints from a variety of journals. The former type of issue, quite apart from its traditional importance in a hospital in which it has long been established, provides a convenient medium for the publication of papers which have a peculiar interest for its alumni, or are unsuitable because of their length or other reasons for the general or special medical journals. The latter brings together the papers published by the hospital staff during the year and shows how diverse is its contribution to research. Probably too it has considerable value in stimulating gifts to the hospital and in gratifying those who have already helped it. Between these are intermediate types. Thus the current number of the *Brompton Hospital Reports* contains three original papers dealing with work done at the hospital and sixteen which have already been published. The republished papers are not mere reprints, however, but have been reset so that the lay-out of the pages is uniform. In the *St. Thomas's Hospital Reports* for 1937 the main mass of the book is taken up with original papers, but at the end there are abstracts of those published by the staff in other journals during the year. Hospitals under local authorities also enter the field. The London County Council reprint annually in the *Archives of Neurology and Pathology* the writings of its staff at the Central Pathological Laboratory at the Maudsley Hospital, and moreover a considerable body of original matter, of general or special medical interest, appears in the various sections of the annual reports of the Council.

Much might be said on the general issue of the choice of "a local habitation" for an account of original work of such merit that it would be not only acceptable but welcome almost anywhere. We commented a few months ago on the quality of the articles in the current *St. Bartholomew's Hospital Reports* and on the small number of subscribers to that journal. Some would say that work printed in a hospital journal remains more or less in hiding; others would protest that only by forcing old students and others to turn to the pages of their hospital reports will the institution receive due recognition and perhaps financial support as the place which provided the facilities for the work done. This may apply particularly to smaller hospitals; the *Royal Berkshire Hospital Reports*, of which the fourth number has just appeared, contains original work of considerable

merit, and it is said rather surprisingly to be intended primarily for circulation to the hospitals' subscribers. Probably the question will decide itself. Few hospitals are likely to follow the example of Guy's and undertake to issue reports quarterly, in which case the staff will perforce publish most of their work outside, though yielding with various degrees of grace to the appeals of the editors for occasional contributions.

EXPERIMENTAL PEPTIC ULCER

PEPTIC ulcer ranks with rheumatism and cancer as one of the common diseases whose causes are still obscure. It looks as if it ought to be a less difficult problem to solve than either of the other two. It is such a consistent well-defined lesion, and we seem able to modify its course considerably by treatment. Yet no infection has been found to account for it and it cannot be attributed to any precise dietetic deficiency. The psychologists would persuade us that emotional disturbances underlie it; but though these are evidently an important factor in the ulcer patient we hesitate to accept them as the whole cause of the disorder. Whatever rôle we assign to constitution or diathesis, we cannot regard that as anything more than a predisposing factor. Yet we feel that a clearer understanding of the causes and even of the pathological mechanism of the chronic ulcer would quickly lead us to means of preventing it.

Some light on the mechanism may yet come from the study of experimental chronic ulcer in animals. This may now be produced in dogs in two ways. The well-known Mann-Williamson procedure is a violent anatomical rearrangement of the gastro-intestinal tract: the pylorus is divided and the upper end of the duodenum closed; the duodeno-jejunal junction is divided and the lower end of the duodenum inserted into the lower ileum, while the pyloric end of the stomach is anastomosed to the upper end of the jejunum. The duodenal juices are thus delivered uselessly into the lower ileum and the animal wastes from interference with intestinal digestion; but in the meantime it almost always develops an ulcer in the uppermost jejunum, just where the acid gastric contents first impinge on jejunal mucosa. A recent study [1] on Mann-Williamson dogs started from the suggestion that gastric ulcer seems to be less common in pregnant women than in the non-pregnant. The pregnancy hormones were therefore given to groups of animals for the weeks following operation. Twelve control dogs all developed ulcers, and fifteen which received 1000 units daily of theelin (œstrin) did likewise; but of fifteen which were given 100 units daily of Antuitrin S, eight developed no ulcers at all and the rest were less severely ulcerated than the controls. Antuitrin S is the "pituitary-like" hormone of pregnancy urine, and any theoretical connexion between it and the jejunal mucosa is at present too remote to be worth looking for. But the experimental results are striking and the observation is obviously worth repeating and following up.

The second variety of experimental ulcer is produced with great regularity in dogs by oral or parenteral administration of cinchophen in doses only a little larger than those commonly advocated in human therapeutics.[2] With the first few daily doses of the drug a diffuse hæmorrhagic gastritis develops, and the dog vomits, passes tarry stools, and loses its appetite. The stomach mucosa shows œdema, congestion and round-cell infiltration, multiple erosions, and small acute ulcers. At the same time the amount of acid juice which it secretes is much increased, though the concentration of acid shows little change. In a week or two this phase subsides, the secretion diminishes, and the mucosal changes regress, leaving, however, one or two ulcers which persist and become chronic. These are almost always situated on the lesser curve near the pylorus, and histologically they closely resemble human peptic ulcers. They may perforate or bleed severely. They last as long as the cinchophen administration is continued and then heal in about three weeks in those dogs that survive. In batches of dogs the number that develop cinchophen ulcers and the severity of the initial gastritic changes can be somewhat diminished by a milk diet, and by large doses of mucin; milk diet with alkali administration prevents the formation of chronic ulcers altogether, but only mitigates the acute changes, and a preliminary gastro-jejunostomy has much the same effect; but animals given histidine hydrochloride develops ulcers with the same regularity and severity as controls. Ulcer does not occur in the antrum when it is surgically isolated from the rest of the stomach and thereby protected from contact with acid gastric secretion. There is thus a remarkable parallelism in behaviour and in structure between cinchophen ulcer in the dog and human peptic ulcer. This is not to say that the human ulcer is caused either by cinchophen or by any other simple chemical poison, but it suggests a state of normal balance between the digestive attack of acid gastric juice and the defences of the gastric mucosa—a balance that is upset in the dog by a poison which damages the defences and incidentally strengthens the attack. If the investigators can go on to discover how it damages the mucous membrane cells, or what is the intimate biochemistry of its action, they may provide clues to the major problem of the genesis of human peptic ulcer.

[1] Sandweiss, D. J., Saltzstein, H. C., and Farbman, A., *Amer. J. dig. Dis. Nut.* 1938, **5**, 24.
[2] Bollman, J. L., Stalker, L. K., and Mann, F. C., *Arch. intern. Med.* January, 1938, p. 119; *Arch. Surg., Chicago*, 1937, **34**, 1172, and 1937, **35**, 290; *Amer. J. dig. Dis. Nut.* 1937, **3**, 822.

EVACUATION OF CHILDREN FROM THREATENED TOWNS

IN a moving plea for plans to ensure the removal of children from the great cities most exposed to aerial attack upon this country, Prof. J. A. Ryle in the *Times* of May 9th offers new constructive suggestions. In his view

the most appropriate and feasible scheme, if the emergency threatens, would be one devised to secure adoption of city boroughs, districts, and streets by counties, small country townships, and villages. For the planning of evacuation coöperation and conference between the education authorities in town and country, existing organizations such as the Children's Country Holiday Fund and the railway companies at once suggest themselves. With schools as collecting and receiving stations, one teacher allotted to every 50 children and one boy scout or girl guide to every 10, marshalling and control in transit should be possible and effective. Arrangements for reception and redistribution to mansion or school or farm or cottage would be the concern of committees in the small towns and villages. Rationing depôts would have to be established in or near the county towns. Each child should have an indestructible label with name and address and registration number and a linen bag containing a mug and a spoon, an iron ration, and, where possible, a change of underclothes. Children of one family should, so far as possible, be kept together—an elementary but important lesson from experience with the

Basque children. The first evacuations should be of children between the ages of five and fifteen. Mothers with smaller children and infants would require a separate organization, but when moved should at least be conveyed to the same county as other members of their families.

The need for careful local investigation and central record of the billeting possibilities in the country districts and of attention to the organisation of transport, commissariat, hygiene, and medical services is not ignored. Prof. Ryle evidently has reason to believe that peace organisations and such bodies as the Society of Friends could be relied on to help in these matters; and he points out that such voluntary participation would not only relieve the Government of a heavy responsibility, but would perhaps be more acceptable to parents than any alternative plan. The arguments for and against closing London schools during the period for which air raids might be expected are well set out in the report made this week to the L.C.C. by its education committee, who give their reasons for favouring a policy of (*a*) evacuation of children to safer districts, and (*b*) immediate closure of all schools on the occurrence of an emergency.

The fact that 4000 Basque children could be brought to this country at short notice and distributed about our countryside encourages the idea that on the principle of adoption might be based a scheme whereby, in a national crisis, our own children could be removed from the dangers of physical injury and the even greater danger of lasting mental trauma.

NURSING CONDITIONS IN L.C.C. HOSPITALS

WHILE other authorities, municipal and voluntary, are busy with shortening the hours of their nursing staffs and increasing the amenities offered to them, the L.C.C. intends on the recommendation of its Hospital and Medical Services Committee to make alterations so far-reaching as to change the whole pattern of the nursing service. A 96-hour fortnight for both day and night duty is to be worked on a three-shift basis with an overlap of shifts in the middle of the day and in the afternoons while lectures and classes are being held. In the general hospitals members of the emergency staff already allocated to each hospital are to supplement the ward staff during the peak hours from 7.30 A.M. to 11 A.M. During normal conditions the hours at fever hospitals will fall into line; for times of epidemic no recommendation is made at the moment. The carrying out of these proposals will involve the employment of about 1000 additional staff at an ultimate cost estimated at nearly £123,000 a year; and nurses experienced in hospital administration are likely to agree that the additional staff required for efficient service will exceed expectations.

If the announcement gives a shock to ratepayers, it may cause even more disturbance to the authorities of voluntary hospitals who are competitors for recruits to a nursing cadre. Those training schools whose prestige rests firmly on a tradition of excellent teaching facilities and of consideration for their staff have little to fear; they will find young women prepared to offer more arduous effort for the privilege of enrolment in their service. But they will be wise not to disregard the other changes contemplated by the L.C.C. in the direction of greater freedom, especially to State-registered nurses. These proposals include, besides liberty to return to hospital at a later hour without having to seek previous permission (State-registered nurses will not be bound even by a midnight curfew), many privileges that will give satisfaction without being very costly. Some of these, such as provision of a special room for games, theatricals, or dressmaking, of weekly periodicals in staff common-rooms and arrangements for enabling nurses to have breakfast or supper in bed on days or evenings off, are already offered by many voluntary hospitals. Facilities for the supply of light refreshments after 10 P.M. for those nurses who have been absent from supper are more rare. A new and a good idea is the provision of accommodation at other hospitals of the Council for nurses who want to spend their free nights in a different atmosphere, and of picnic meals for others who propose to make expeditions to the country on their free days. Those who have long advocated a readjustment of conditions of hospital service to meet the changed outlook of the modern girl will welcome all these amenities and the reduction of hours of work. The ultimate effect of the adoption of the three-shift basis of service is less certain. THE LANCET Commission on Nursing recorded the success of this experiment in New Zealand and elsewhere abroad and in some hospitals at home, but did not anticipate its general adoption here "at any rate for some time." Their survey was indeed deliberately restricted to a search for desirable adjustments without fundamental change in the present system of hospital staffing. But they noted the main advantage of the three-shift system: it obviates the need for complicated schedules of off-duty time and shortens the span of work, since the nurse's eight hours on duty are consecutive, broken only by meals. The fact that the application of this system to domiciliary nursing would gravely disturb the conditions of employment of private nurses is no argument against its trial in institutions where the shortage of recruits has now become so acute that drastic changes of policy are inevitable.

EXCLUDING TUBERCLE FROM THE SERVICES

THE remarkable extent to which the radiological examination of the chest has come to be considered essential in any scheme for testing the fitness of applicants for public service is indicated by a study in the *Revue de la Tuberculose* for March by A. Bidermann and A. Alibert. The French law of March 30th, 1929, made obligatory the examination by a specialist in tuberculosis of every applicant for an administrative appointment under the State. No applicant could be accepted unless he were found to be free from tuberculosis by a clinical and radioscopic examination supplemented, if necessary, by a radiographic examination. Since 1933 the radioscopic examination of the chest has been systematically practised in the French army and in many other services. Bidermann and Alibert have studied three important services, those of the railways, police, and State. Their conditions are in some respects dissimilar, the health standards required of the police being particularly high. Of the 24,827 candidates for employment by the railways during the three-year period 1935–37 297, or 1·2 per cent., were discarded on radiological evidence. This comparatively low ratio reflects the fact that the persons radiologically examined had all been passed as sound after a clinical examination which, when it had revealed definite evidence of pulmonary tuberculosis, had rendered a radiological examination superfluous. Another qualifying fact to be noted is that the radiologists did not discard those applicants whose radiological shadows could be interpreted as harmless though possibly tuberculous. The radiological examination of 2066

would-be policemen led to the discarding of only 19, or 0·9 per cent. But of this group it must be said that they were hand-picked beforehand, having served in the army and having been examined by the chief medical officer of the prefecture. The third category represented less select material, the applicants for administrative employment by the State belonging to both sexes and, in most cases, not having undergone a general medical examination beforehand. Several of the men had not undergone military service. Of the 1891 applicants radiologically examined 30, or 1·6 per cent., were discarded on the radiological report. Since the institution of routine examination of applicants for these various services there has been a great decline in the percentage of discards: in the case of the police from 1·8 per cent. in 1933–34 to 0·5 per cent. in 1936–37. This decline is to a certain extent the measure of the popularity of the radiological examination which weeds out more and more radiologically positive persons before ever they come to the final examination for service. Only a few years ago persons conscious of a tuberculous past would take the chance of its being undetected by the medical examiner, whereas at the present time the prospect of a radiological examination deters many a gambler from such a chance. The State employee who develops tuberculosis is now given sickness benefit on a generous scale, and the State is naturally anxious to avoid many such calls; what it spends on radiological examinations by experts is a trifle compared with what it saves by the timely elimination of tuberculous applicants.

BACTERICIDE WITHIN THE BODY

IT is only six years since the synthesis of Prontosil and only three since its remarkable antibacterial properties were first disclosed. Since then the stream of chronicles, critical or merely descriptive, of the successful use of this drug and of its derivative sulphanilamide has swelled to a river so full and so fast that none but an expert could plunge his way through it and survive to comment sanely on his experience. The definite knowledge accumulated about this group of drugs has been masked by publications which are either speculative, statistically vulnerable, or so irrelevant as to merit little attention. The fact that most of the early work on the subject in this country appeared in our columns makes them an appropriate place for an assessment and we therefore invited Prof. Garrod to undertake this arduous task. He introduces his masterly survey (see p. 1125) of the results of this method of treatment by tracing its development and considering its mechanism. He discusses absorption, circulation and excretion, choice of compound and dosage, and begins a review of therapeutic action which this week is confined to the various streptococcal infections. In a concluding article next week he will discuss the effect of this group of drugs on infections due to certain other organisms, their use in prophylaxis, their local application under certain conditions, and their toxic effects.

The section to which we would direct special attention in the first part of this survey is that on mode of action. Prof. Garrod shows that this is no longer "an astonishingly efficient mystery" though it is not yet completely cleared up. And he emphasises again a point which though often made is not always taken: that the use of these drugs, which is not without its dangers, imperatively demands a bacteriological as well as a clinical diagnosis. They are specific not for septicæmia, meningitis, or pneumonia but for infections by certain bacteria wherever situated, while on other species they have little or no effect.

MARRIAGE GUIDANCE CLINIC

A MEETING will be held at the Caxton Hall, Westminster, on Thursday, May 19th, at 5.30 P.M., to discuss the tentative programme put forward by the committee which has been formed under this name to carry on the work of the marriage committee of the British Social Hygiene Council. It is proposed that the new committee should be controlled by an independent governing body drawn from among medical, scientific, educational, social, and religious workers. Its aims are to give preparation for marriage through lectures and private consultations, and to build up gradually a body of people qualified to deal with problems in marital relationships. If the work of this voluntary committee is proved to fill a need it is hoped it will ultimately be recognised as a necessary part of national schemes of preventive medicine. The chairman of the provisional committee which has been appointed is the Rev. A. Herbert Gray, and the vice-chairman is Mrs. L. Blackett Jeffries, M.D. Among the medical names on the advisory board are Lady Barrett, Dr. Gladys Cox, Dr. Ethel Dukes, Dr. Frances Huxley, Dr. Joan Malleson, Dr. Emanuel Miller, Dr. J. R. Rees, and Dr. Henry L. Wilson. Further information may be had from the secretary, Mrs. M. C. Hume, 13, Wildwood-road, London, N.W.11.

THE next session of the General Medical Council will open on Tuesday, May 24th, at 2 P.M., when Sir Norman Walker, the president, will deliver an address.

A NUMBER of subjects bearing on medical research are to be considered by the section of chemistry at the British Association's meeting at Cambridge in August. In a discussion on repercussions of synthetic organic chemistry on biology and medicine Prof. E. C. Dodds and Prof. L. Ruzicka (Zürich) will describe work on the production of new compounds having the biological action of the sex hormones, and Mr. A. S. Parkes, F.R.S., will deal with some of their interesting biological interrelationships. The programme will also include descriptions of synthetic compounds that are able to produce cancer (Prof. J. W. Cook, F.R.S.), of new compounds having the physiological action of the life-maintenance hormone of the adrenal cortex (Prof. T. Reichstein, Zürich), and of the synthesis of vitamin B_1 and analogous compounds (Mr. A. R. Todd, Ph.D.).

EDUCATION IN THE OPEN AIR.—Speaking last Saturday at the opening of the Hayling Island Open-air School established at the sea-side by the Tottenham local education authority, Mr. Kenneth Lindsay, parliamentary secretary to the Board of Education, said that the number of open-air schools had increased from 7 in 1910 to 153 to-day, with accommodation for something over 16,000 children, and 33,500 children had passed through them last year. The open-air school was not merely a school in the open air; it comprised a way of life and a system both of educational and medical supervision, characterised by fresh air and sunlight, a proper and sufficient diet, healthful and adequate rest, a hygienic way of life, from regular bathing to participation in formal physical training, medical treatment, individual attention, and special educational methods.

The Tottenham authority have provided the new premises, at a cost of some £30,000, and the school accommodates 120 children, half of whom are sent by other authorities.

SPECIAL ARTICLES

THE CHEMOTHERAPY OF BACTERIAL INFECTIONS

By LAWRENCE P. GARROD, M.D., F.R.C.P.

BACTERIOLOGIST TO ST. BARTHOLOMEW'S HOSPITAL; PROFESSOR OF BACTERIOLOGY IN THE UNIVERSITY OF LONDON

IT has long been believed that bacterial infections differ from protozoal in being by nature insusceptible to chemotherapy. Apart from the action of Novarsenobenzol in anthrax, and the clinically inapplicable treatment of experimental pneumococcal infection with Optochin, the only site in which bacteria have been found vulnerable by systemic chemical attack is the urinary tract, and here conditions are peculiar. This situation has been radically altered by the discovery of Prontosil and the studies which have ensued from it. The known effective scope of treatment with this and allied compounds is widening rapidly, and while in several directions most brilliant success has already been achieved, so much ground remains to be explored that the ultimate consequences of this discovery are beyond prediction. It is the purpose of the following review to assemble information on this subject, which exists for the most part only in scattered form, and particularly to assess the value of the treatment in each of those diseases in which it has been tried. The literature of the subject is already so extensive that few are in a position to assimilate it except in predigested form.

It is necessary to a proper understanding of this treatment first to trace its development and to consider its mechanism.

Discovery of Prontosil

It is only just to acknowledge that the credit for what is perhaps the greatest discovery in modern therapeutics belongs entirely to the staff of the institute of experimental pathology and bacteriology of the I. G. Farbenindustrie, Elberfeld. Others have contributed largely to its extension; workers in France provided the clue to the secondary discovery of the action of sulphanilamide, and valuable studies both of the action and of the mode of action of these drugs have been carried out here and in the U.S.A., but it was the original German discovery that pointed the way to these efforts. Sulphamido-chrysoidin (prontosil) was synthesised by Mietzsch and Klarer in 1932, and its properties were first generally disclosed by Domagk [39] in 1935. During this long interval it had evidently been placed in the hands of practitioners in the Rhineland for clinical trial, and early reports such as those of Foerster [51] and Grütz [68] might have indicated to anyone with a careful eye on the German literature that something new was brewing. The facts revealed by Domagk, and subsequently by Hörlein [82] in the English medical press, were these. Prontosil was one of a number of azo compounds which had been tested for antistreptococcal activity in mice in the course of a prolonged research previously embracing organic compounds of gold. It was almost non-toxic, and pharmacologically inert in the sense that blood pressure, unstriped muscle, and the integrity of blood-vessels were unaffected by it, but mice inoculated intraperitoneally with 10 minimum lethal doses of *Streptococcus pyogenes* survived if from 1/10 to 1/50 of the maximum tolerated dose were administered repeatedly either orally or by injection. Staphylococci were also susceptible to its action: pneumococci and other species of streptococci than *S. pyogenes* were not. This action in mice had been confirmed in man by dramatic results in the treatment of streptococcal infections; Domagk's original paper is immediately succeeded by two others describing such results.

These experimental observations were confirmed by Levaditi and Vaisman [86 97 99] and by Nitti and Bovet [123] in France and by Buttle * and by Colebrook and Kenny [30] in this country, after a short period of doubt attributable to the use of different strains of streptococci. It soon became evident that the most striking results were obtainable with streptococci of high mouse virulence, and this apparent anomaly depended on the fact that a minimum lethal dose contained only a small number of cocci; it is a peculiarity of prontosil, evidenced in other ways, that it acts best on a sparse and scattered bacterial population, and not on highly concentrated masses of bacteria.

SULPHANILAMIDE

Prontosil is entirely without action on bacteria in vitro, and its mode of action in the body was an almost complete mystery until Tréfouël, Tréfouël, Nitti, and Bovet [158 159] put forward the hypothesis which launched an immense volume of effort in a new direction. Arguing by analogy with a much earlier observation by Heidelberger, and by comparison between therapeutic activity and the constitution of a number of different azo compounds, they concluded that activity resided in that part of the molecule which consisted of a sulphonamide group attached to one benzene nucleus. Assuming that sulphamido-chrysoidin (prontosil) in the body is split at the double bond, but without proving that this is so (a task later carried out by others), they proceeded to test the therapeutic action of one component which would thus be liberated, and found it equivalent to that of prontosil itself. Thus began the study of *p*-aminobenzene sulphonamide (first abbreviated to "sulphonamide" but now known as "sulphanilamide"). This compound is not only therapeutically effective, but it has an action on streptococci and other bacteria which is demonstrable in vitro. It remained for Fuller [56] to prove that sulphanilamide is formed in the body when prontosil is administered; this he did by studying the urinary excretion of the drug in mice. In the normal animal only about one-quarter of the prontosil given appears in the urine as sulphanilamide, in the infected animal nearly one-half; excretion is also slower in the presence of infection. These differences remain unexplained, but it may be pertinent to them that Long and Bliss [105] claim to have demonstrated a reducing action on prontosil exerted by streptococci themselves.

This further very promising discovery, coupled with the fact that sulphanilamide was not protected by patents, led rapidly to its widespread manufacture and use, particularly in this country and the U.S.A.

Composition and Nomenclature

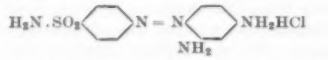
Sulphanilamide is marketed under a number of proprietary names, some of which afford a clue to its identity, while others appear quite meaningless. It is to be hoped that manufacturers gain some advantage from this practice commensurate with the confusion which it causes. This multiplicity of

* See *Lancet*, 1935, **2**, 840.

names, together with the advent of further new compounds chemically related to sulphanilamide, make it necessary to define the substances with which we are dealing. An account of wider efforts to synthesise new compounds will be given later; the following are those which have been used in therapeutics :—

Prontosil (originally known as Streptozon; subsequently as Prontosil rubrum, Prontosil flavum, or Prontosil):

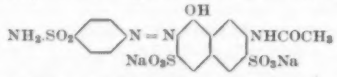
4'-sulphamido-2 : 4-diaminoazobenzene hydrochloride.



Given by mouth only; the preparation with which many early studies were done, but now much less often used.

Soluble prontosil (Prontosil solubile: marketed by one firm in U.S.A. as Prontosil).

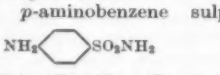
The disodium salt of 4' sulphonamide-phenyl-azo-1-oxy-7-acetylamino-naphthalin-3 : 6-disulphurous acid



Given by intramuscular injection. (It is to be understood that when "prontosil" is said in this paper to have been given by any parenteral route, this form of the drug is meant.)

Rubiazol, the French equivalent of prontosil, which owes its manufacture in France to the exemption of medicaments from patent law in that country, had originally the same composition [99] as the German product, but the name now denotes a compound with an added COOH group.[141]

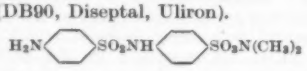
Sulphanilamide: *p*-aminobenzene sulphonamide



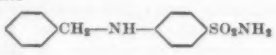
(marketed as Sulphanilamide, Prontosil album, Sulphonamide-P, Streptocide, Prontylin, Colsulanyde, Sulphamidyl, &c.). Given by mouth, by subcutaneous injection, and intrathecally.

The three other compounds for which therapeutic data are available are :—

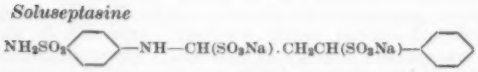
Uleron (DB90, Diseptal, Uliron).



Proseptasine



Soluseptasine



It is to be noted that most of what follows does not necessarily apply to any of these substances; what is known of their properties will be mentioned separately.

Absorption, Circulation, and Excretion

The only full pharmacological study hitherto published is the valuable work of Marshall, Emerson, and Cutting [106 107 108] and concerns sulphanilamide only. These authors have shown by repeated estimations of the drug in the blood that it is rapidly absorbed from the gastro-intestinal tract, this process being complete within 4 hours, and that it enters the circulation at the same rate if given subcutaneously. Reaching a peak in about 3 hours, the concentration falls in a straight line to almost zero in 24 hours; this means that a fully adequate amount for therapeutic action persists after any single dose for about 6 hours; 4 or 6 hourly administration will therefore maintain this. This persistence in the blood is clearly an important factor in success; other substances theoretically capable of chemotherapeutic action, such as acridine compounds, are so rapidly eliminated that an adequate blood level is not maintained. Marshall and his colleagues claim to have shown that this persistence in the blood is due to the reabsorption in the renal tubules of 70–80 per cent. of the sulphanilamide in the glomerular filtrate. In the same experiments the rate of clearance was found to be independent of the plasma level, but to increase with the rate of urine flow; (the knowledge that the drug can be washed out of the circulation by forced fluids and consequent diuresis may be utilised in over-dosage accompanied by toxic effects). These workers also estimated the drug in various organs, and found the concentration everywhere the same but for a diminished amount in bone and fat; it appears that sulphanilamide is uniformly distributed in the water of the body. They demonstrated its presence in pleural and peritoneal effusions, saliva, pancreatic juice, and in the cerebro-spinal fluid. In this last and most important situation serial estimations in the dog, in a normal man, and in a patient convalescent from cerebro-spinal fever all gave similar results; the curve of concentration paralleled that in the blood at about three-quarters of the blood level. These findings differ from those of Jauerneck and Gueffroy,[86] according to whom excretion into the cerebro-spinal fluid may be delayed, more so in the normal individual than in the presence of meningitis. This discrepancy calls for further study; frequent comparisons of the blood and C.S.F. concentrations during treatment for meningitis are desirable.

Sulphanilamide is wholly excreted in the urine, where it appears in both free and conjugated form. Excretion is delayed when the kidneys are previously damaged. It has already been mentioned that prontosil is excreted in the urine partly unchanged and part as sulphanilamide. The general behaviour of all these compounds in the body is probably similar, but studies such as those described have not been published in connexion with any compound other than sulphanilamide.

Choice of Compound and Dosage

It will save repetition to summarise the general results of clinical experience on these points. With exceptions, which will be noted later, sulphanilamide receives an overwhelming vote as the most generally useful drug, and oral administration, when feasible, serves all purposes except perhaps the immediate treatment of meningitis, when intrathecal injection of a 0·8 per cent. solution in saline may be desirable. This solution may also be given subcutaneously, if necessary in large volumes (700 c.cm. has so been given as an initial dose) when swallowing or alimentary absorption is at fault. An alternative in these circumstances is to inject prontosil soluble intramuscularly (intravenous injection of this compound is unnecessary and badly tolerated and intrathecal is dangerous). Most authors agree that a large initial dose is desirable (of sulphanilamide from 3 to 5 g.) in order to attain an adequate blood level as soon as possible; Long and Bliss [105] suggest an estimation of the blood content four hours later; if this should be below 10 mg. per 100 c.cm. subcutaneous injection is indicated. Further doses should be given 4-hourly. Long and Bliss in this and another paper [102] discuss dosage fully, and adopt

the rule for total daily dosage of 1 g. sulphanilamide per 20 lb. of body-weight (maximum 5 g.) and 1 c.cm. prontosil soluble (2·5 per cent. solution) per 1 lb. (maximum 120 c.cm.). These doses, especially of sulphanilamide, have often been exceeded, though a dose of over 7 g. daily is uncommon. Children require a 50 per cent. larger dose in proportion to body-weight than adults.[103] These maximum doses should be stepped down at two- or three-day intervals in favourable cases.

This scheme applies to gravely ill patients; for less serious cases half this dosage or less may be enough. Opinion on the advisable duration of the treatment has not yet crystallised, but there is much to be said for limiting a course to ten days, and only resuming it, if necessary, after an interval. What these drugs can do they usually will do within that time or less, and fatal agranulocytosis is a possible consequence of prolonged administration.

Mode of Action

The intelligent use of any drug demands that its mode of action shall if possible be understood, since special circumstances may arise in which such knowledge alone can dictate the right course to adopt.

It is perhaps scarcely necessary to point out that the use of these drugs imperatively demands a bacteriological as well as a clinical diagnosis. They are specifics not for septicæmia, meningitis, or pneumonia, but for infections by certain bacteria wherever situated, while on other species they have little or no effect. They interfere in some way with the activities of these bacteria in the body, and the question is, how?

Some of the most successful forms of chemotherapy are imperfectly understood, and for a time after Domagk's original announcement prontosil was simply accepted as an astonishingly efficient mystery. How it was first postulated and then proved that prontosil liberates in the body the substance now known as sulphanilamide, which has a demonstrable effect on bacteria, has already been related. Two other experiments may here be mentioned which bear on this point; whereas prontosil has no effect on streptococci in vitro, it was reduced with the aid of magnesium powder by Colebrook, Buttle, and O'Meara [29] and with cysteine hydrochloride by Bliss and Long [9] to something, presumably sulphanilamide, which was bacteriostatic. The former authors also describe the first detailed experiments illustrating the effect of sulphanilamide on streptococci in vitro. A concentration of no more than 1 part in 18,000 (i.e., less than that attainable in the blood) prevented the growth of *small numbers* of streptococci (a few hundreds or perhaps thousands per c.cm., but not the millions introduced by an inoculum of undiluted culture). This action was most marked in blood, and much more so in human or monkey blood than in that of the rabbit or mouse; it was also obtained in serum, and to a less extent in broth. Among other authors [104 124] who have confirmed these observations, only Hoare [80] has amplified them significantly. He finds that the blood of patients taking prontosil or sulphanilamide is actually bactericidal to streptococci; that this effect is not the so-called Tillett phenomenon [156] is evidenced by similar effects obtained with normal blood and equivalent added sulphanilamide. The blood may assume this property within 1 hour of administration or only after some delay; this difference is attributable to variation in the rate of absorption.[81] Of 21 strains of *S. pyogenes* tested in normal blood with added sulphanilamide, all but 2 were destroyed, and these came from cases which had not responded to sulphanilamide treatment (it is noteworthy in this connexion that a similar relationship between resistance in vivo and in vitro has been observed by Bliss and Long [11] among serological groups of *S. pyogenes* and by Felke [49] among different strains of gonococci). Substitution experiments showed that no change in the leucocytes of treated patients was responsible; the active agent was in the serum. Sulphanilamide was also bactericidal in serum alone, but this effect required doubled concentrations (optimum 1 in 8000, that in blood being 1 in 16,000, with lesser effects in each case up to one-eighth of these).

These are formidable facts, and strongly support the simplest explanation of the whole problem—namely, that sulphanilamide has a direct damaging action on streptococci, either actually killing them, or at least preventing their growth; the limited numbers upon which the drug acts in vitro correspond to those found in the blood-stream and elsewhere in widespread infection. Bacteriostasis, which if complete must ultimately result in the victory of the bodily defence mechanism, is the explanation accepted by Bliss and Long [10] and by Gay and Clark.[58] The latters' work and that of Mellon et al [115] indicates that there is no stimulation of the defence mechanism, in the sense of any altered behaviour on the part of leucocytes.

This general view, although widely accepted here and in the United States, has been strongly contested on the Continent. Its principal opponent is Domagk [40 41 42] himself, who is unwilling to relinquish the idea that prontosil has an action per se, apart from that of the sulphanilamide which it liberates. Perhaps the most solid argument in favour of this idea is that weight for weight prontosil is therapeutically the more effective; the amount of sulphanilamide which it liberates is distinctly less than the amount of sulphanilamide itself which has to be given to achieve the same result. Other arguments adduced by Domagk are the variability of effect in different animals (inconsistent for evident reasons with the supposition of a simple action on bacteria), discrepancies between in vivo and in vitro effects (to be discounted owing to the unduly heavy inoculum used in his vitro tests), and the fact that other therapeutically active compounds such as Uleron are not reduced to sulphanilamide in the body. This last point, also emphasised by Levaditi,[95] seems to me to have singularly little force; no one wishes to maintain that sulphanilamide is the only directly active compound in the series, nor need it be supposed that other colourless compounds require conversion to it; the question at issue is whether the azo linkage of prontosil has to be broken to secure activity. Opposition in France to the English-American view has taken the form of propounding several highly speculative alternative hypotheses. Levaditi and Vaisman [97] believe that prontosil prevents capsule formation by streptococci, so rendering them susceptible to phagocytosis; Mayer [112 113] and Levaditi [94] postulate the conversion of sulphanilamide itself in the body into some other and more active substance (Levaditi's crucial experiment in support of his belief in this matter has been repeated by Colebrook [28] with an opposite result), while Levaditi and Vaisman [98] also claim to have proved that prontosil neutralises streptococcus toxins (leucocidin and hæmolysin). Meyer [117] also reports experiments in which hæmolysin was neutralised or its formation prevented, and Osgood [127] observed the absence of hæmolysis in streptococcus cultures containing sulphanilamide. I believe this

phenomenon to have little practical significance; in my experience many antiseptics which have no chemotherapeutic action will inhibit hæmolysis in culture when present in concentrations insufficient to prevent growth. I can also add to the evidence on this aspect of the subject the personal observation that prontosil does not neutralise Dick toxin.† Gley and Girard [62] claim that exposure in vitro to either prontosil or sulphanilamide diminishes the virulence of streptococci; this is unconfirmed.

It is still open to anyone to believe either that the action of these drugs is simple or that it is complex. If the former, they are simply antiseptics effective in vivo; if the latter, then some of the more speculative conclusions here quoted may prove to embody some aspect of the truth.

Therapeutic Action

STREPTOCOCCAL INFECTIONS

The action of these compounds in the majority of hæmolytic streptococcal infections is now a matter of almost universal experience, and not one demanding proof. In the following analysis, therefore, only a selection of the more significant published experiences will be quoted. It is important first to recognise that susceptible infections are only those due to *Streptococcus pyogenes*; those due to *S. viridans*, such as subacute bacterial endocarditis, and to *S. fæcalis* (urinary tract infections due to this organism) are uninfluenced. Even within the present rather wide scope of the term *S. pyogenes* there are resistant types. Bliss and Long,[11] having failed to cure 4 cases of urinary infection by hæmolytic streptococci with sulphanilamide, ascertained that these streptococci were of Lancefield's serological group D; subsequent studies of bacteriostatic action in vitro showed that whereas groups A and C are fully susceptible, the effect on groups B, E, and G is variable, while on D there is none. Fortunately from this point of view, almost all serious infections in man are due to members of group A.

While there are several valuable reports [69 102 104 154] embracing a variety of streptococcal infections, it will be more convenient to deal with these conditions separately.

Erysipelas.—There is almost complete unanimity on the uniformly good effect secured in this disease. In most of the more extensive series of published cases [3 9 16 118 151] prontosil was the drug used, and its action has been compared with that of other remedies such as ultra-violet light and antitoxin. Spread is usually arrested forthwith, and fever often abates within 24 hours. It may be that erysipelas is pre-eminently amenable to treatment owing to the vascularity of the lesion, which allows full access by a remedy circulating in the blood; the conditions are certainly much more favourable than in, for example, an abscess or a septic thrombus. The only adverse reports on the treatment are those of Hartl,[72] who saw no good effect at all (possibly because he used the intravenous route) and Angerer [2] who makes a distinction between simple and complicated cases; in the latter, where erysipelas was superimposed on some other condition or vice versa, no less than 26 of his 38 cases died.

Tonsillitis and scarlet fever.—Many authors mention favourable results in acute tonsillitis and pharyngitis, but extensive studies are few. Gallagher [57] used sulphanilamide in an epidemic, and concludes that adequate dosage hastens the disappearance of streptococci from the throat, wherein he differs from Smith,[150] in whose experience cases recovering after treatment with sulphanilamide or proseptasine remained carriers for several weeks. Gallagher mentions that his routine included forced fluids; this measure is incompatible with fully efficient sulphanilamide treatment, since, whatever else it may do (itself perhaps a matter meriting critical inquiry) it hastens the elimination of the drug itself. I have been unable to find any record of an adequate study of the action of sulphanilamide in scarlet fever. Peters and Harvard [131] treated 150 cases with Proseptasine; the duration of fever was slightly longer then in 150 control cases, and the frequency of complications was somewhat less.

Otitis media and meningitis.—These may rightly be considered together, since almost all the streptococcal meningitis treated has been otogenic. Hageman and Blake [68] record that under sulphanilamide treatment otitis media usually subsides without discharge and mastoiditis without operation. In streptococcal meningitis the effect obtained has evidently astonished those who have witnessed it. There is no doubt that this disease, once almost invariably fatal, is amenable to treatment, but there is still uncertainty how best to administer it. Flake and Carey,[50] whose 4 cases all recovered, gave sulphanilamide intrathecally as well as subcutaneously and by the mouth. Neal and Appelbaum [121] also used the intrathecal route, but appear doubtful of its necessity; 13 of their 17 cases recovered. Schwentker et al.[147] treated 4 cases, 3 recovering, with prontosil and sulphanilamide given variously. Trachsler et al.[157] who had 7 cases with 4 recoveries, and Weinberg et al.[162] with 2 successful cases, used prontosil intramuscularly and sulphanilamide orally, avoiding the intrathecal route; Cawthorne [26] is also doubtful of its value. It seems generally agreed by those who have injected 0·8 per cent. sulphanilamide in saline intrathecally that this proceeding is free from danger, but prontosil given in this way has caused violent febrile and local cellular reactions.[119 147]

Puerperal fever.—The extensive and careful studies made in the Isolation Block of Queen Charlotte's Hospital are familiar to readers of this journal, and need only be summarised briefly. Owing to the previous existence there of a full service for the ætiological as well as therapeutic study of puerperal fever on a large scale, the material and the means were available for a therapeutic trial more complete than has yet been possible in many conditions other than puerperal fever. The earlier reports by Colebrook and Kenny [30 31] deal with a total of 64 cases treated with prontosil; more recently Colebrook and Purdie [32] have described the effects in 106 cases of using sulphanilamide. This has been given orally, sometimes in very large doses (up to 15 g. daily in severe cases), or by intravenous drip in cases vomiting. Among the prontosil-treated cases there were only 3 deaths, and in the sulphanilamide series 8, due mainly to causes outside the influence of the treatment, such as pulmonary or cerebral embolism and hæmorrhage. The mortality of streptococcal puerperal sepsis, previously 20 per cent., has thus been markedly reduced, and comparison and analysis are used in every possible way in these papers to distinguish therapeutic effect from a possible diminution in the natural severity of the disease. If the invasive capacity of *S. pyogenes* is indeed undergoing spontaneous diminution, cases with proven septicæmia cannot be considered to have gained advantage from this, and it is therefore highly significant that the mortality among such cases, previously 71 per cent., has fallen to 27·3 per cent. Gibberd,[60] analyses the same cases by a method similar in principle; including only those in which infection spread beyond the uterus, and excluding deaths, he found a distinct shortening in the average time of illness; the frequency of general peritonitis was also greatly diminished. The present view taken at Queen Charlotte's Hospital is that the effect of prontosil in severe cases is slightly superior to that of sulphanilamide. A striking report from elsewhere is that of Foulis and Barr [53]; among 22 severe cases, 11 having

† The neutralisation tests in human skin on which this statement is based were made with concentrated toxin kindly supplied by Dr. R. A. O'Brien.

septicæmia and 3 peritonitis, only 1 died; the majority were treated with large doses of sulphanilamide only, 7·2 g. being sometimes given daily for a week or more.

Other streptococcal infections.—The treatment has been used successfully in various other conditions, including streptococcal pneumonia or empyema, burns, and cellulitis. An adequate series of wound infections is lacking; this would be of interest, since there are indications that connective tissue infection responds less readily than, for instance, erysipelas.

(To be concluded)

UNITED STATES OF AMERICA

(FROM OUR OWN CORRESPONDENTS)

THE BROADCAST ON RHEUMATISM

AT 7.30 P.M., eastern daylight saving time, this day (May 2nd) we heard Lord Horder opening the first international health broadcast on the subject of rheumatic heart disease. His voice came to us every bit as clearly as the voices of the following American speakers from San Francisco and Atlantic City.

NEW FOOD AND DRUG LAW

President Roosevelt has approved a bill giving the Federal Trade Commission jurisdiction over foods, drugs, diagnostic and therapeutic devices, and cosmetics. This law provides that unfair and deceptive acts and practices in the exploitation and sale of foods, therapeutic drugs and devices, and cosmetics in interstate and foreign commerce are to come under the bureau of the commission sixty days after signing. The control of the commission over unfair acts and practices is limited to those which constitute or form unfair methods of commercial competition, including the advertising which is disseminated in interstate or foreign commerce. Only in event of proved danger to health will the offender be liable to fine or imprisonment. A "false advertisement" within the meaning of the act is any advertisement, other than labelling, that is misleading in a material respect. In the case of a drug, no advertisement is to be considered false that is disseminated only to members of the medical profession, contains no false representation of a material fact, and includes or is accompanied in each instance by a truthful disclosure of the formula, showing quantitatively each ingredient. The provisions of the act which relate to advertising originated in bills designed to safeguard the public against fraud and danger to health through the distribution in interstate and foreign commerce of adulterated and misbranded foods, drugs, diagnostic and therapeutic devices, and cosmetics. The advertising of foods, drugs, &c., is therefore vested in the Federal Trade Commission, while jurisdiction over the labelling of such products is to be left with the Secretary of Agriculture, and there will be a similar division of authority with respect to the general control of such merchandise. While it is possible that the new act will lead to some improvement, the division of authority is not in general looked upon with enthusiasm.

CONFERENCE OF STATE HEALTH OFFICERS

The health officers of the several States met in Washington on April 9th–11th with the provincial health officers of Canada for their annual conference. Dr. F. W. Jackson, deputy minister of health of Manitoba, spoke of the attitude of the Dominion toward the provision of medical care. He was supported in the discussion by Dr. R. E. Wodehouse, deputy minister of health for Canada, who aligned himself with the recommendations of P.E.P. for the extension of the health insurance principle. Dr. R. G. Leland presented the point of view of the American Medical Association, contrasting "a constantly improving system of free and independent medicine, consistent with American principles and traditions and in accordance with the ideals and traditions of centuries-old medical ethics," with the state of affairs in foreign countries which have established systems of medical practice "dominated and controlled by the State." His fear for the future is well expressed in the following paragraph.

"If incursions into the field of medical practice are to result ultimately in supplanting the private practice of medicine, and if physicians should ever become mere robots, making diagnoses from card indexes and mechanical gadgets, and prescribing treatment from already prepared and numbered labels, and should patients become a mere collection of interesting human parts to be shunted from one corner to another of a medical repair shop for some heartless and pseudoscientific tinkering, America will have lost one of its greatest institutions—free and independent medicine; and the American people will have lost some of their most valuable human traits—confidence in, respect for, and reliance on the scientific men and women who now endeavor to protect their health and prolong their lives. It is doubtful whether refinements of administrative methods or improvement in public health technique can ever replace or compensate for such a public loss."

Dr. W. C. Woodward, formerly health officer of the District of Columbia, supported the position of Dr. Leland, and expressed the view that, if adequate incomes were available to the mass of the people, sickness caused by poverty would be eliminated and the purchase of adequate care would be possible. Surgeon-General Parran said that the growth of medical knowledge had increased the cost of applying the sum total of that knowledge for the benefit of the patient, and good medical care was beyond the reach of an increasing number of persons. Half of all illness was among the very poor, one-fourth in families actually on relief. More than half a million persons in the United States were unemployable because of accident or disease, much of it preventable. It was not only humane but good business to provide for a national health programme which must be adaptable to the varying needs of the State and community. Our ability to prevent disease far exceeded our ability to control the causes of poverty. Medicine, he said, can give hope and confidence to an age almost despairing that man's intelligence will keep us from reverting to barbarism.

REDUCTION OF PNEUMONIA MORTALITY

Dr. Joseph W. Mountin, of the U.S. Public Health Service, exhibited charts illustrating the great variation of pneumonia mortality in different areas of the country, the highest figure being found in three areas: the Colorado plateau, the Atlantic seaboard, and the Appalachian highlands. He outlined a programme of epidemiological research in which a bacteriological study will be made on clinical cases and carriers for a period of 12 consecutive months. In each centre of investigation, preferably a city of considerable size, the sample is to include not less than 1000 clinical cases whose sputum and blood will be examined for diagnostic purposes. Investigation of carriers

will be made through the culturing of nose and throat of some 1000 cases, half of which would have had recent contact with a clinical case. The service is in a position to finance 5 study units during the ensuing year. Each State health department is advised to set up a special unit on pneumonia control. In the discussion Dr. Edward S. Godfrey, Jun., of New York State, pointed out that the mere distribution of serum cannot of itself be expected to control mortality from pneumonia. The typing of the higher series of pneumococci demands quite special skill. Laboratory technicians must be thoroughly trained and the work of the laboratory supervised. Nor can it be assumed that the general practitioner is an expert in serotherapy. In New York State post-graduate courses in pneumonia control are now available and the response has been enthusiastic.

THE TAVISTOCK CLINIC

THE annual meeting and luncheon of the Tavistock Clinic was held on May 9th at the Café Royal. Lord ALNESS, the newly elected chairman of council, invited Sir HENRY BRACKENBURY, the retiring chairman, to say something about the work of the clinic. Three important aspects of that work, Sir Henry said, were continuity, variety, and volume. Since the clinic was founded nearly 20 years ago by Dr. Crichton Miller the work had expanded enormously, but the missionary spirit in which it was founded had continued. In spite of the increase of work, all those engaged in it were anxious that nothing should be done to lower its quality. The clinic had moved to larger premises and hoped in time to come to move to still larger ones. The care of the patients treated called for a large staff and large premises, as well as a few small wards. There was immediate need for support of the current work of the clinic; they could not go on facing an annual deficit of several hundreds of pounds, without being forced to retrench. He suggested that all donors should make a 50 per cent. increase in their gifts for the next two years.

Mr. WALTER F. ROCH, honorary treasurer to the clinic, contributed a sorrowful account of the clinic's finances during the past year. A deficit of £3500 had been met by selling all realisable assets and by a reduction of honoraria to the medical staff; indeed they had now qualified as a sweated industry. If the clinic had been a commercial concern, the outlook for the future would be excellent: the work was expanding, its quality was recognised, and the clinic occupied a good site with ample room for future extension. But unfortunately the clinic was not a commercial enterprise and increasing work meant increasing debts. The council must look for an ever-increasing flow of contributions.

The CHAIRMAN thanked Sir Henry for his thought-provoking and informative speech and urged all those present to spread the evangel of the clinic. He was a hard-worked chairman, for at the luncheon which followed he welcomed the guests and introduced the Earl of FEVERSHAM, Parliamentary Secretary to the Ministry of Agriculture and Fisheries. Nobody, Lord Feversham said, liked to see a valuable asset turned into an expensive liability to the State. He had worked as a probation officer and had concluded that crime was an external expression of a deep-seated psychological cause. In his present occupation he was dealing with sub-human species, but he believed that to see nature in the raw you must turn to man. He hoped that in the next generation the work of the clinic would be apparent in a lower incidence of breakdowns and neurotic conditions.

Mrs. ISRAEL SIEFF paid a tribute to Sir Henry Brackenbury who, she said, had guided the clinic through lean and hungry years. The work of the clinic showed that 50 per cent. of neurotic conditions could be cured or permanently relieved, and she thought this no mean achievement for a branch of medicine in the pioneer stage. There were some invalids who inspired confidence and happiness in those about them, but the neurotic was not among these. The neurotic spread unhappiness. A profound relaxation of tension was experienced by those families in which a neurotic had been restored to mental health.

Dr. J. R. REES, medical director of the clinic, mentioned the closed waiting-list of the clinic, with 400 names upon it. How many of those patients, he wondered, would have committed suicide and how many would have to be certified before treatment could begin for them. Psychoneurotics had been estimated at 7 per cent. of the population; that is to say, if anyone wrote down the names of the first 14 of his friends who came into his head, he would find at least one who could do with some readjusting. Follow-up work at the clinic showed that 50 per cent. of patients were permanently improved, and among children this figure rose to 70 per cent. He urged those present to help to keep this work alive and effective.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED APRIL 30TH, 1938

Notifications.—The following cases of infectious disease were notified during the week: Small-pox, 0; scarlet fever, 1936; diphtheria, 1055; enteric fever, 20 ("expected" 27); pneumonia (primary or influenzal), 1270; puerperal pyrexia, 182; cerebro-spinal fever, 32; acute poliomyelitis, 5; acute polio-encephalitis, 1; encephalitis lethargica, 7; dysentery, 37; ophthalmia neonatorum, 121. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on May 6th was 4917, which included: Scarlet fever, 808; diphtheria, 1056 (carriers 49); measles, 1718; whooping-cough, 295; puerperal fever, 18 mothers (plus 12 babies); encephalitis lethargica, 282; poliomyelitis, 1. At St. Margaret's Hospital there were 23 babies (plus 9 mothers) with ophthalmia neonatorum.

Deaths.—In 126 great towns, including London, there was no death from small-pox or enteric fever, 35 (7) from measles, 4 (2) from scarlet fever, 12 (2) from whooping-cough, 26 (2) from diphtheria, 37 (10) from diarrhœa and enteritis under two years, and 63 (8) from influenza. The figures in parentheses are those for London itself.

Measles proved fatal in 21 great towns, Hull having 3 deaths. Liverpool reported 4 deaths from whooping-cough. Diphtheria was fatal in 21 great towns, none reporting more than 2 deaths. There were 11 deaths from influenza in Birmingham, 4 in Hull, 3 in Bristol.

The number of stillbirths notified during the week was 300 (corresponding to a rate of 39 per 1000 total births), including 40 in London.

TYPHOID AT HAWICK.—More than 50 cases of typhoid have occurred at Hawick, a parliamentary burgh of 17,000 inhabitants in Roxburghshire. The cases are widely distributed over the town, a large proportion of them being women. No deaths have been reported. The water-supply was overhauled a few months ago and the cause of the outbreak has not been ascertained. The usual precautionary measures have now been taken.

OPENING OF THE NEW WESTMINSTER MEDICAL SCHOOL

ANOTHER step towards the completion of the Westminster Hospital was taken on May 12th when the Earl of Athlone opened the new medical school. The school occupies one-third of the block on the west side of St. John's-gardens in Horseferry-road, the other two-thirds being taken up by the nurses' hostel which was opened in March. The hospital itself is on the east of the gardens and will be ready for occupation in April of next year. For 52 years the medical school was in Caxton-street where it moved after leaving its first home through the construction of Victoria-street. Since 1903 its students have done their preclinical work at King's College. The completion of the new buildings will finally remove the inconvenience of geographical separation of the school from the clinical material of the hospital.

The new school is an eight-storied building which will provide the student with opportunities for rest, recreation, and exercise, as well as education. His bodily needs will be catered for particularly in the basement, in the ground floor, and on the roof, while the rest of the building will be dedicated to his mental improvement. On the ground floor there is a comfortably furnished common room, a refectory on the cafeteria system where 80 students at a time can be served from the adjoining kitchens of the nurses' hostel, a smoking room, and a small bar. In the basement is a billiards room, a gymnasium, and a squash rackets court, with the necessary shower baths and rooms for changing and drying clothes. In the summer the student will be able to study or rest from his labours on the flat roof.

The main lecture theatre which seats 250 occupies the depth of two floors, with entrance on the ground floor, and contains a film projector and epidiascope of the latest type. Most of the first and mezzanine floors are taken up by the library and museum, the latter having a gallery in which microscopical preparations are displayed. On the second floor is the main class room with its desks set in tiers so that everyone has an uninterrupted view of the blackboard and projector screen, and on this floor also is the class preparation room and a smaller lecture theatre to seat 50. The third and fourth floors contain the pathological laboratories and workshops, both for teaching and the routine work of the hospital. The main clinical laboratory, named to commemorate the generosity of John Burford Carlill, is divided into cubicles for individual workers and is provided with a built-in refrigerator room and one maintained at body temperature.

On various floors there are rooms for the examination of patients and for special tests on the living subject, in the design of which special care has been

taken to ensure seclusion, so that emotional disturbances may be eliminated as far as possible. The biochemical laboratory is on the fifth floor and on the sixth is the physics department with research rooms and the laboratory for the special study of radium emanations. Here too is a large room for

operative surgery and an anatomical museum for advanced students. Finally, the seventh floor is mainly given over to the research workers. In addition to their laboratories and separate library there is an X ray plant for the examination of post-mortem specimens and for pathological research and the apparatus for clinical photography and photo-micrography.

The entire cost of the school is being met by a fund distinct from that raised for the rebuilding of the hospital and nurses' hostel, and subscriptions are urgently required to meet the £15,000 still outstanding.

GRAINS AND SCRUPLES

Under this heading appear week by week the unfettered thoughts of doctors in various occupations. Each contributor is responsible for the section for a month; his name can be seen later in the half-yearly index

FROM "SILVER DOCTOR"

II

HOW IT GOES

Opsonins neglected, vaccines past their best,
Serums still in some demand, hormones in request,
Vitamins are booming and a necessary pest,
But endocrines are all the rage to activate the rest.

WHAT is the explanation of the sudden cardiac deaths which occur nowadays so frequently, and not least among our own profession? Is coronary thrombosis more common or only more exactly diagnosed than heretofore? What is its immediate cause? There always has been an element of mystery about blood-clotting, and modern biochemistry does not explain entirely its whys and wherefores. Diseased blood-vessels do not appear to be the complete answer. Does the modern increase of cigarette-smoking and/or motor-exhaust fumes play any part? Now then cardiologists, what about it?

* * *

Recently a fresh spate of cheap wit has poured contempt on the "bedside manner." Assuredly there was a time when undue importance was attached to externals in the relation between doctor and patient. This was a relic of the days when medicine was confused with magic, and its professors sought to dazzle their dupes by an atmosphere of mystery. To-day medicine has emerged into the light as a science and an art, doctors are recognised as nothing more and nothing less than trained experts, and frock-coats have gone the way of gold-headed canes. Once and forever we have exploded any idea that fine feathers make fine medical birds. Yet I suggest that the pendulum has swung too far and too fast, and that there is, and always must be, the need for a properly conceived "bedside manner." A patient comes to a medical man to discuss symptoms which may involve the most intimate matters and any or every consultation may deal with questions of life and death. The doctor's ability to help remains the same whether he is clad in the latest thing in morning-coats or a dilapidated suit of fishing-kit. Yet an element of anxiety is inseparable from every consultation and this demands recognition. Seemliness is a constant in the transactions of civilised life and nowhere is it more deeply rooted than in the British character. Every patient is influenced by impressions derived from external appearances, and such details as clean hands, spotless linen, quiet clothes, and a sympathetic manner go far to ensure a patient's confidence. Even to-day it is not everyone who appreciates the smell of tobacco, yet how many practitioners ignore this. Clothes certainly do not make the man; yet it is equally certain that coloured pull-overs, grubby collars, and grimy flannels are out-of-place in the sick-room, and there was a sting in the saying of one patient about doctors that "by their hands ye shall know them"! Recently I heard a surgeon pour scorn on the "waste of time" involved by the ancient custom of inspecting the tongue and feeling the pulse. Even if this performance taught nothing (a ridiculous suggestion) it gives a patient the opportunity to note the manner of man to whom they are entrusting their lives. No time is wasted which is spent in examining a patient or hearing his story, yet how often we forget that he is not the least interested in our family triumphs, our views on Art, or our golfing successes. Self-consciousness is a crime in any doctor, and the man who is so good-looking or so ugly that he cannot forget it is of little use in our job. It may not be given to every practitioner to possess the personality which appeals to the sick man, but he should cultivate those lesser graces which reassure the invalid. A "bedside manner" founded on these ideals is the bounden duty of every doctor.

* * *

As a guess I suggest that "three times a day" is one of the most familiar phrases of our mother-tongue, associated by millions of English-speaking people with a doctor's instructions. Every type of patient—fat or thin, male or female, old or young, black or white; each dilapidated organ—liver, lungs, heart, nerves, tummy; all alike are doomed at some time or other to a recurring potion three times a day. Maybe this was all very right and proper in days gone by, yet in the name of Hippocrates himself why this everlasting *three*?

One pictures the original doctor of all time confronted by his first patient. Did he then and there with one almighty brain-wave conceive the three-fold function? Or was it as the outcome of trial-by-error experiment with hourly, daily, or weekly doses of apple-extract or fig-leaf decoction that the fiat went forth to echo down the centuries "three times a day"? Maybe there is more in this *3* business than appears at first sight. Everywhere the magic figure turns up. Why do we call for *3* cheers, or in superlative moments *3* times *3*? Who ordained that the drowning subject should come *3* times to the surface? Why is the *3rd* time proverbially "catching-time"? Was it a coincidence that Jonah spent *3* days and *3* nights in the whale's interior? Why *3* blind mice and *3* men in a boat? Why did the poet sing "Of the three hundred grant but *3* to make a new Thermopylæ"? Is it conceivable that not arithmetic alone but the universe itself revolves round a *rule of three*?

However its origin and whatever its past virtues, doctors follow too slavishly this ancient custom. The "thrice daily" business has become an obsession. House physicians and clinical assistants in hospital are prone to order every patient his three daily doses as a matter of routine, while the average practitioner is apt to conceive that his duty begins (and sometimes ends) with a similar performance. No wonder

nowadays that nurses and patients alike are unsatisfied unless and until the threefold ritual is enacted. The thing has grown into a habit.

Dogma dies hard, and "something out of a bottle" is still the constant demand of many invalids. Doctors must preach *and practise* in and out of season that drugs are not required in every case. To-day there is over-much playing with palliatives, and a real danger of forgetting the usefulness of such measures as routine, rest, exact diet, periods of starvation, planned exercises active or passive, bath treatment in its many forms, cuppings, counter-irritation, and the like. In acute cases drugs should be given at short intervals for a definite period and stopped when the required effect is obtained. In more chronic affections drugs may be necessary for a longer time, but in many of these one or two doses in each 24 hours is often sufficient. Placebos have a limited usefulness but the unwholesome clamour for the medicine bottle must be checked. The army of unnecessary drug-takers is a pitiful reproach to our profession, who alone can dispel the delusion that t.d.s. is the sure road to health.

* * *

In January's Grains and Scruples A Bacteriological Back-number discussed the pros and red-inked the cons of artificial immunisation with the pen of a master. My own communication is privileged by virtue of a comparative ignorance. As an honest clinician I hesitate to venture into such deep waters, but a sense of duty urges the record of a personal hair-raising experience. That it concerned the injection of a curative rather than an immunising serum is a mere quibble. The serum's the thing. A Bacteriological Back-number sounds a warning of the dangers of serum injection in no uncertain words when he writes "no method involving a parenteral injection is without a significant risk and when injecting a healthy individual with anything we are always skating on thin ice." Here is a case when the ice gave way to a tragedy.

While staying recently in an hotel I received an S O S from a colleague in an adjoining suite. There I found a distressed doctor performing artificial respiration on a young woman to whom a few minutes previously he had given an injection of antidiphtheritic serum. The patient had been under observation in bed for two days with sore-throat, fever, enlarged glands, and a suspicious tonsillar patch. She collapsed within two minutes of the injection. The girl was unconscious, white, pulseless, and gasping. Adrenaline, brandy, strychnine, and artificial respiration proved of no avail and twenty minutes later she was dead.

Subsequent investigation threw little light on the exact cause of this distressing catastrophe. Nothing was found wrong with the serum, its dosage, or the details of its administration. The girl was organically sound, she had never had any previous injection, nor was there the history of asthma or other allergic manifestation. She had not seemed seriously ill. Most tragic of all, the subsequent bacteriological examination of a throat swab (very properly taken before injection) proved the absence of diphtheritic bacilli. The death certificate was worded "tonsillitis, serum injection, anaphylaxis, cardiac failure," though "medical misadventure" would have been equally truthful.

It is not pleasant to reflect that this tragedy was the direct result of medical treatment and that we are largely in the dark as to how and why she died. Such deplorable accidents fortunately are rare and are not always published. I record the case, firstly because of an uncomfortable conviction that the present generation of practitioners and medical students is not sufficiently alive to a terrible possibility, and secondly as an urgent plea for renewed research into the mysteries of acute serum reactions.

It is essential to preserve a due sense of proportion. There is no question of the overwhelming benefit of serum treatment and the small proportion of its disasters, yet however rare these may be they cannot but make us think. Anaphylaxis is a comfortable long word which covers a wealth of ignorance. Its minor manifestations are comparatively common. Surely these should serve as a basis from which to evolve its essential nature and how it may be avoided, while the modern frequency of blood transfusion ought to aid in a similar direction.

MEDICINE AND THE LAW

Lead Poisoning and Water-supply

LAST week the Court of Appeal confirmed a decision whereby at Manchester assizes a plaintiff and his wife were awarded damages for lead poisoning due to drinking the water supplied by the Irwell Valley Water Board. The trial judge had held that the defendants fulfilled their statutory duty of supplying pure and wholesome water in their mains. But the water, being soft, was plumbo-solvent; it absorbed lead from the service pipes in the plaintiff's house. The defendants had failed in their common-law duty to warn consumers that they must take precautions because the water had a capacity to absorb lead from leaden service pipes. The defendants, it appeared, had adopted measures for hardening the water. There had been about six cases of plumbism in a population of 16,000 during the six years before the hardening plant was installed. After the installation no further cases occurred.

The Court of Appeal emphasised that the defendants had been repeatedly warned of the risk that their supply would be contaminated before reaching the consumers. There were complaints by consumers from 1929 to 1935; but it was a long time before any measures were taken to make the water harmless. The water board could easily have taken one of two steps. It could either have adopted some method of reducing the plumbo-solvency of the water, or it could quite simply have sent consumers a circular warning them to draw off a certain quantity of water which had been standing in the pipes before using the water for drinking purposes. The water board, through its agents, had been negligent. Lord Justice MacKinnon pointed out that the defendants knew a great deal about the risk of plumbo-solvency; yet they had exposed their consumers to the danger without warning. Scientific knowledge on these matters, he said, had greatly advanced in recent years. In 1902 the Local Government Board held an inquiry into the plumbo-solvency of moorland water-supplies. As a result in various local Acts of Parliament there have been inserted special provisions requiring water undertakings to treat the soft water. A common-form clause insists that, if it appears to the undertakers that the water supplied is "liable to act upon lead in such a manner as to endanger the health of the consumer," they must forthwith treat the water so as to prevent such action. The county medical officer of health is sometimes authorised by such clauses to take steps to secure the necessary treatment, and there is sometimes a statutory penalty of £5 for every day during which the undertakers make default in complying with the requirement.

CORRESPONDENCE

BLOOD PRESSURE IN SCARLATINAL NEPHRITIS

To the Editor of THE LANCET

SIR,—In his paper in your issue of April 30th (p. 999) Dr. R. Workman Carslaw, from his experience of 50 cases of scarlet fever, came to the conclusion that it was impossible to diagnose early post-scarlatinal nephritis by daily blood-pressure readings. This conclusion is confirmed by my observations many years ago[1] when I published a paper on blood pressure in scarlet fever based on the study of 122 cases. Of the 33 cases in this series which developed nephritis only 12 showed any hypertension, which was never extreme or of long duration, while in the remaining 21, whose ages ranged from three to twelve years, the systolic blood pressure did not rise above 110. The absence of any rise of blood pressure in many cases of post-scarlatinal nephritis and the large number in which only a slight and transient rise was noted are in keeping with the fact that scarlatinal nephritis is as a rule a benign affection, the great majority of such cases ending in complete recovery. In the early days of clinical sphygmomanometry T. Janeway,[2] like most physicians interested in the subject, hoped that it would furnish most important indications in acute infectious disease. Some years later,[3] however, he had to confess that that hope had been disappointed. "I think," he wrote, "that most of us must now agree with the conclusions of Kurt Weigert from his extensive studies of the acute infections, and which have been confirmed for scarlet fever by Rolleston, that the value of the blood-pressure measurement for prognosis in the acute infectious diseases is slight. It is an additional factor which is occasionally useful, as in typhoid patients with hæmorrhage, but for the most part the simpler observations made by our predecessors in clinical medicine of the facies, the tongue, the pulse, and the heart sounds, and the state of the nervous system, make the prognosis equally well without a knowledge of the blood-pressure curve."

I am, Sir, yours faithfully,

London, W., May 7th. J. D. ROLLESTON.

TESTOSTERONE PROPIONATE, THE ANTERIOR PITUITARY, AND HYPERTHYROIDISM

To the Editor of THE LANCET

SIR,—In your issue of Feb. 12th I reported that the male hormone, testosterone propionate, if given in adequate doses, renders the endometrium atrophic. But it remained doubtful whether it acts on the endometrium itself, on the ovarian follicle (antagonising the female hormone), or on the sexual motor, the anterior pituitary. To answer this question I ascertained the amount of gonadotropic hormone in the urine in women receiving testosterone for hæmorrhage at the menopause, and found that under treatment it either disappeared or diminished, according to the dosage. This demonstrates that testosterone acts through the pituitary—a conclusion supported by the observation of J. B. Hamilton and J. M. Wolfe (*Endocrinology*, March, 1938,) that in rats it suppresses production of gonadotropic substances by the pituitary.

If, indeed, the male hormone blocks the production of gonadotropic hormone by the anterior pituitary it may also interfere with the action of the other anterior pituitary hormones, such as the thyrotropic, adrenotropic, and growth factors. Accordingly, on the assumption that hyperthyroidism may be caused by excessive secretion of thyrotropic hormone, testosterone has been tried in Graves's disease, and I am able to report the first success with this remedy.

The patient, a girl of 14, is being treated by Dr. S. F. Seelig in St. John's Hospital, Lewisham, London, according to my suggestions. She had conspicuous exophthalmos, a diffusely enlarged thyroid, excitability, tremor, and a pulse-rate of 150. She had lost weight during the last few months and was suffering from insomnia; rest in bed with administration of bromide and phenobarbitone failed to bring the slightest improvement. Under the influence of 850 mg. of testosterone propionate, given over a period of two months, the thyrotoxic symptoms diminished considerably. Although the patient was not kept in bed, and received no drugs, her weight increased, the pulse-rate dropped to 84, the tremor became hardly visible, and the exophthalmos lessened. Excessive perspiration vanished and she became much calmer. The treatment began on March 1st and improvement has continued from that time onwards.

Though it is too early to judge of the permanence of the cure, the evidence of this case suggests that testosterone propionate can be used to reduce excessive thyrotropic activity on the part of the pituitary gland. The effect of the treatment was to perform a partial temporary functional hypophysectomy. In my latest cases I have found that this effect can be attained not only by injecting the male hormone, but also by rubbing it into the skin. The percutaneous dose corresponds to the dose given intramuscularly. The results of the above investigations were reported by me to the International Congress of Obstetrics and Gynæcology held in Amsterdam last week.

I am, Sir, yours faithfully,

London, W., May 10th. ALFRED A. LOESER.

PYLORIC STENOSIS IN TWINS

To the Editor of THE LANCET

SIR,—Dr. Sheldon's interesting paper in your last issue illustrates two common fallacies in twin research, which tend to bring the method into disrepute. Under the title "Hypertrophic pyloric stenosis in one of uniovular twins" he mentions that 22 out of 23 twin pairs were discordant for this disease, and that the number of twins in his material was unduly large. Since roughly one-third of all twins are monovular, and since on the basis of a single Mendelian recessive a quarter of the binovular male pairs ought to be concordant, the obvious deduction is that even in this tiny sample some 7 twins with faulty genes have failed to develop the disease. The case report which is given supports this deduction and the general impression left by the article is that in the ætiology of pyloric stenosis important environmental factors are involved which, since we are dealing with twins, *must be extra-uterine.*

Such a conclusion is quite unjustified on the evidence presented. Assuming for the purpose of simplification that pyloric stenosis occurs only in male infants, and making one or two other minor adjustments, the following calculation is sufficiently accurate. In 2000 births there will be 25 twin births producing 4 pairs of uniovular males, the same number of binovular male pairs, 8 pairs of unlike sex, and 8 female pairs. Among 1000 male infants selected

[1] *Brit. J. Child. Dis.* 1912, **9**, 444; Acute Infectious Diseases, 2ED, 1929, p. 271.
[2] Clinical Study of Blood Pressure, 1904.
[3] *Bull. Johns Hopk. Hosp.* 1915, **26**, 348.

at random from an infinite population there will be 8 uniovular and 8 binovular twins (each with a brother who does not come into the sample), and 8 binovular male twins with a sister, 24 twins in all, a number which agrees with Dr. Sheldon's 23. Admittedly Great Ormond-street does not draw on an infinite population, but between 1912 and 1936 sufficiently large numbers are involved for this to be a negligible source of error.

It is the sex distribution of Dr. Sheldon's material, however, that should have warned him that something odd was happening. Whereas there ought to be twice as many twins with brothers as twins with sisters, actually there are as many, or more, pairs of unlike sex. This type of distribution is a common one: it is usually ascribed to the fact that when both twins do badly the feeding or some other environmental factor is blamed; when only one infant does badly the mother rightly argues that the fault lies in the baby and goes to a clinic straight away without wasting time experimenting.

These 23 pairs of twins are thus a grossly selected sample, about 10 pairs being missing. One inference is that most of the missing pairs were uniovular and binovular concordant.

The second fallacy in Dr. Sheldon's paper is the proof of monozygotism in the case reported in detail. Binovular twins frequently share a placenta, just as monovular twins often have separate ones. The decisive point is that when there is a common placenta the circulations of monovular twins anastomose and under these circumstances the birth-weights tend to differ, one twin or other having an advantage. The common placenta with agreement in birth-weights is therefore an argument against monozygotism, just as is the disagreement in finger-prints. In fact in the teeth of the objective evidence, on the strength of a subjective impression of resemblance without any of those corroborative details which an expert would provide, we are asked to believe that of two twins with an identical genetical composition and an identical blood-supply (which appears to have been so evenly distributed that the birth-weights agree) one twin is exposed to an environmental factor at birth or soon after, which the other avoids, and that this factor acts so quickly that within a few days signs of stenosis develop.

Dr. Sheldon may be quite right; if he is, his observation is of unusual importance because it is possible to exclude the intra-uterine differences so often present in the case of monovular twins. At any rate he owes it to the many scientists who will read his paper with interest to find someone with a hand-lens and a knowledge of skin genetics who will confirm or disprove the diagnosis of monozygotism.

I am, Sir, yours faithfully,

Oxford, May 8th. DENYS JENNINGS.

AN OVERCROWDED PROFESSION?

To the Editor of THE LANCET

SIR,—May I revert to the letter signed M.D., M.R.C.P., which appeared in your issue of April 30th? This letter suggested that the Medical Peace Campaign is proposing that refugees should be free to enter this country and to fill posts in an already "overcrowded profession." No such proposal has been made by the Medical Peace Campaign. In an earlier issue (March 26th) of this journal appeared a letter, signed by a number of distinguished medical men, which expressed the hope that some support might be given to our colleagues excluded from their posts in Austria. I am confident that the signatories had no intention of prejudging the case raised in our own country by the presence of refugees. It is in the opinion of our committee a problem that requires earnest discussion by the whole profession; and, appreciating that the Austrian coup d'état was associated with a display of armed force, we decided to republish the letter for wider distribution.

I am, Sir, yours faithfully,

W. HOWARD HUGHES.

St. Mary's Hospital, W., May 9th.

HEARING-AIDS FOR DEAFNESS

To the Editor of THE LANCET

SIR,—Further to Mr. Macleod Yearsley's letter, I would like to point out that, following research carried out at Manchester University by Drs. Littler and Ewing, they state in their pamphlet "Auditory Fatigue and the Use of Tuned Telephones with Hearing Aids," on p. 7:

"Recently we examined the records of 10 unselected children who have used hearing-aid apparatus similar to that employed in our speech experiments daily for periods of two years and upwards. They were tested with a pure-tone audiometer both at the beginning, at intervals, and at the end of a period. In none of these cases had any falling off in acuity occurred. In some instances the test results were better at the end of the period of using the hearing-aid apparatus."

Then we read in the National Institute for the Deaf's pamphlet, "The Choice of a Hearing Aid" (p. 3):

"There appears to be no clinical or experimental evidence that the continued use of a hearing-aid causes any increase in existing deafness nor, except in a few rare cases, does it improve or restore hearing. Nevertheless, the benefits from a satisfactory and appropriate instrument are very definite both to the patient and his friends."

I may be wrong, but I believe this is also an extract of opinion from the same source as the one given earlier. There would also seem to be reason to think (not, unfortunately, clinical or scientific evidence) that cases are not entirely unknown where the use of a hearing-aid has actually so far assisted the function as to result in the discarding of this assistance after some months, as redundant.

No one can quarrel with Mr. Yearsley's second point that it is the duty of an aurist to send his patient to an "honest" firm. It is the greater pity that so distinguished an aurist has not gone a little further with his investigations however. To send a patient to a surgical instrument maker is to send him to a selling agent (sometimes one buying such aids through the second-hand columns of the *Exchange and Mart*) instead of to the manufacturer and "specialist" (in the lay sense of that abused word). It must be agreed that the surgical instrument firms are not likely to attempt exploitation, but the system of permitting trial for two or three weeks is full of pitfalls, and actually results in many who could have been satisfactorily fitted being "sent empty away," too often convinced that their case cannot be assisted. Moreover, it should be remembered that those agents who charge the *officially recommended* 5 per cent. of the cost of the aid under trial, can "turn over" the initial cost of that aid in a short period—and still have it on their hands for further unsatisfactory "trial" at the same time.

Now, we find the late Prof. Fraser-Harris saying in your columns (*Lancet*, 1934, **2**, 481):

"Strange as it may appear, there is no body of persons who are qualified to interpret an aurist's prescription for a deaf patient, and to supply the

appropriate deaf-aid instrument, as there are opticians able to read an oculist's prescription and to provide the spectacles specified. Just as it requires a specialist—the oculist—to ascertain the precise nature and amount of departure from normality in vision, so it requires a skilled person to ascertain the precise kind and degree of deafness from which a deaf patient may be suffering. There are types and degrees of deafness just as there are types and degrees of departure from normal visual acuity."

Is not the inevitable conclusion that the time has arrived for an effort to be made to form a corporate body corresponding in aims and training to that of the opticians? It should have recognised examinations, so that aurists and physicians can know when they are recommending their patients for the fitting of an aid that they are in effect recommending a man qualified by training and experience to undertake the task. It is, of course, assumed that such a body would have ethical ideals and would take steps to see that these were lived up to by those entitled to use such qualifications. Such a move would be welcomed by the reputable and experienced firms of standing.

I am, Sir, yours faithfully,

Gt. Ormond-street, W.C., May 4th. L. T. E. WEBB.

OBITUARY

ARTHUR PEARSON LUFF, C.B.E., M.D., F.R.C.P. Lond.

Dr. Arthur Luff, who died at Limpsfield on May 1st aged 82, was a notable member of the chain of physicians attached to St. Mary's whose contributions to forensic as well as to clinical medicine have brought renown to the hospital.

Born in London, the son of Richard Luff, and educated at the Western Grammar School and the Royal College of Science, A. P. Luff taught chemistry for some years before taking his B.Sc. in 1883, having been awarded the Pereira medal of the Pharmaceutical Society in 1874. In 1883 he gained the gold medal of the Society of Apothecaries of London in materia medica and pharmaceutical chemistry. He proceeded to study medicine, qualifying L.S.A. and M.R.C.S. Eng. in 1886 and M.B. Lond. in 1887 with high honours. In the same year he was made lecturer in forensic medicine at St. Mary's, and he continued to hold this post for 21 years, during which period he wrote a two-volume text-book on the subject and, jointly, a very successful manual on chemistry for medical students. As was natural, Dr. Luff's interest remained chiefly in the chemical and toxicological aspects of medico-legal work. As scientific analyst to the Home Office (1892–1908) he figured prominently in many famous criminal cases of poisoning. His gift of precision in the statement of his opinions in the witness-box and elsewhere brought him as much medico-legal work as he could spare time for. As toxicologist he took some part in the discovery of arsenical poisoning as the cause of an outbreak of peripheral neuritis which in 1900 affected the beer-drinking community of Manchester and Salford, an investigation which has since become something of a classic. He remained in touch with developments in toxicology after his retirement from clinical practice, and served on the Departmental Commission on Preservatives and Colouring Matter in Food in 1923.

In clinical medicine Dr. Luff acquired high repute especially for his art in relieving patients afflicted with various forms of chronic painful and crippling disorders. Having taken his M.D. in 1889, he was appointed assistant physician to St. Mary's in 1890, and full physician in 1896, the year of his election to the fellowship of the Royal College of Physicians. His Goulstonian lectures in 1897 on the pathology and treatment of gout were followed by many other publications on gout, chronic rheumatism, and, later, on fibrositis. He was bold enough to give morphia for acute gout at a time when this drug was withheld in that condition for fear of its effect on renal function and this merciful practice soon became general. It was his exceptional ability to make patients comfortable even when he was unable to make them better that brought Dr. Luff well deserved popularity as a physician. He achieved such outstanding success as a consultant that he felt able to cut short his career in 1913 and retire to the country with the intention of devoting his leisure to his favourite pastimes of golf and carpentry. The war brought him back to work on the medical staff of the Third London General Hospital at Wandsworth, and he was mentioned in dispatches for his services as a lieut.-colonel in the R.A.M.C. (T.). Though he returned to country pursuits on demobilisation he acted some years later as honorary director and rapporteur of some collective investigations on varicose ulceration, the after-history of cases of gastro-enterostomy and cancer of the breast which were sponsored by the British Medical Association. The results were published between the years 1928 and 1932.

Dr. Reginald Miller writes: "Dr. Luff's skill in the management of gouty and rheumatic patients, in the days when everything was either gout or 'goutiness,' quickly gained for him a large and fashionable consulting-room practice, and his success was a source of legitimate satisfaction to him. He was kind and most courteous in manner, but was punctilious in matters which he thought affected the prestige of a consulting physician. He was most precise in his methods and made somewhat of a fetish of punctuality. His hospital work was carried out with the utmost regularity, and his arrivals and (still more wonderful!) his departures were timed to the minute. To be late for an appointment with him was to miss the pleasure of seeing him, and many a practitioner was disconcerted to find that after five minutes' grace he had left the house at which a consultation was due. It is a pleasure, even to those who recall him only as a senior member of the St. Mary's honorary staff, to feel assured that the great content which his success in practice had brought to him remained with him during many years spent in retirement."

Dr. Luff married in 1893 Amy A. Leon and had a son and a daughter, Dr. Mary Luff.

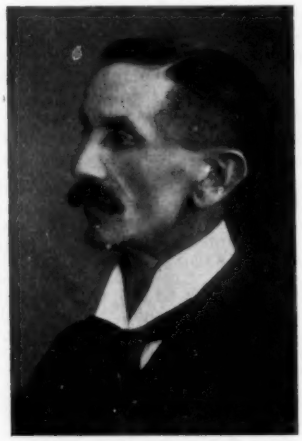
EDMUND WILKINSON, F.R.C.S. Eng., D.P.H.

LIKE so many men of his time who joined the Indian Medical Service, Colonel Wilkinson had a distinguished career in India, and after retirement from the service an aftermath at home of influence and importance. Born in 1867 and qualifying from University College Hospital, London, in 1888, he entered the I.M.S. three years later, after holding a series of resident appointments. On military duty in the Punjab he came up against the recrudescence of bubonic plague and became an authority on its

epidemiology. He was in succession chief plague medical officer, sanitary commissioner in the Punjab, and acting sanitary commissioner for East Bengal and Assam. He was the author with C. W. Daniels of a manual of tropical medicine and hygiene. On retirement from the service in 1914 he joined the staff of the Local Government Board. "Here," writes Sir Arthur MacNalty, "his plague experience proved invaluable, not only in port sanitary work but especially in the precautions against the spread of plague by rats in East Anglia. During the late war he secured a large measure of liaison between the military and civil authorities in the arrangements for military camps and hospitals. After the war he was chiefly occupied in port work and investigating epidemic outbreaks. On leaving the Ministry in 1932, Colonel Wilkinson returned to his native Cornwall to administer his estate and live the full life of a country gentleman. He was a good shot, a keen fisherman, and an ardent motorist, snatching time from his many other occupations for colour photography. At Hornacott Manor, near Launceston, his wife and he were always ready to welcome old colleagues. Death met him with mental and physical powers but little impaired."

PERCY FURNIVALL, F.R.C.S.Eng.

THE announcement of the death on May 3rd of Mr. Percy Furnivall, consulting surgeon to the London Hospital, brought distress to a still wide circle of medical friends, though it is 19 years since he retired from practice. Born in London in 1868, he was the only son of the late F. J. Furnivall, Ph.D. He was educated at University College, London, and received his professional training at St. Bartholomew's Hospital, qualifying in 1892 and taking his F.R.C.S. Eng. in 1895, after varied experience in resident posts at St. Bartholomew's and elsewhere. He was elected to the surgical staff of the London Hospital and continued in office as assistant surgeon and then surgeon until ill health caused his resignation from the active staff in 1919. For some years he acted also as surgeon to St. Mark's Hospital for Diseases of the Rectum and to the Metropolitan Hospital. Mr. Furnivall was awarded the Jacksonian prize of the Royal College of Surgeons for an essay on neoplasms of the stomach, small intestine, and colon in 1898, and in 1901 lectured as Hunterian professor on the same subject. He was co-editor with his father of "Thomas Vicary's Anatomie of the Bodie of Man," and wrote the articles on stomach, intestine, and rectum in the second edition of the treatise on the Operative Surgery of Malignant Disease edited by his father-in-law, Sir Henry Butlin, besides other contributions to the surgical and pathological literature of his day.



[Photograph by Elliott & Fry

We are indebted to Dr. Lewis Smith for the following graphic account of Mr. Furnivall as surgeon and friend: "I met Furnivall first when he joined the London Hospital staff, where his outstanding personality, surgical skill, and general charm ensured his popularity. He was a fine figure, long and lean—6 ft. of wire and whipcord—black-haired and swarthy as a gipsy; he was always cheery, a good mixer, with an unending fund of stories. As a student he won honours as a boxer, and in 1885 was amateur champion bicyclist at various distances. In later years he was a keen golfer and a devoted motorist. 'Furni' was a fine surgeon, with a quick brain; a fearless operator but careful and thorough in every detail. Furnivall said what he meant bluntly and meant what he said; he was a good friend, the most loyal of colleagues, an awkward opponent, and one of the worst correspondents in the world. He was an omnivorous reader and a connoisseur of the good things of life. Recurring bronchial catarrh prevented overseas war service and eventually drove him into retirement in Devon, whence of late years he fled to warmer climates for the winter months. Furnivall was ever a man of action and I doubt if he appreciated the comparative calm of retirement. I visited him on several occasions and in 1931 we met unexpectedly in New Zealand. While in Jamaica in February, 1937, he developed an epithelioma of his left tonsil and with characteristic energy left for New York at once, where he underwent treatment by operation, X rays, and radium. All went well until his return home where in July he began to suffer most painful and distressing after-effects of treatment, graphically described in a memorandum published in the *British Medical Journal* in February last. This letter excited widespread interest and initiated a correspondence which has only just come to an end. In his last letter to me, dated March 1st, 1938, he wrote: 'I've had a grim year but I mean to make the gradient.' But he just missed it. He was a grand fighter, and we could do with more of his type to-day."

THE LATE DR. GRABHAM

Dr. Michael Grabham, whose death we announced on April 23rd, was born in Madeira in 1866, the son of Michael Grabham, M.D., and Mary Anne Blandy. He was educated at University College School, London, and St. John's College, Cambridge, where he was an exhibitioner. Having taken a first in the natural sciences tripos, he went to St. Thomas's Hospital, qualified in 1891, and entered the government medical service in Jamaica. For the next 38 years he had charge of the Victoria Jubilee Lying-in Hospital at Kingston; he was made secretary for the Medical Council in 1894, served on the commission on Cattle Diseases (1895) and the Malaria Commission (1908), received the thanks of the government for his work in the earthquake of 1907, and retired in 1929. His special interests were in tropical diseases and in obstetrics; during his term of office at the Victoria Jubilee Hospital more than 400 maternity nurses were trained for the colony. He contributed many notes and much material to the Carnegie Institution in Washington, which were incorporated in "The Mosquitoes of North and Central America and the West Indies," published by that institution in 1915. After the great earthquake he received a cable inquiring for the safety, not of himself but of his collection of mosquitoes, suggesting that it was too valuable to leave in an earthquake

zone. A genus of more than 40 species of mosquitoes bears his name.

After retiring, Dr. Grabham left Jamaica and returned to his old home in Madeira, where his father remained until his death three years ago. He took great pleasure in botanical work and published in 1934 "Plants Seen in Madeira." Another book on the Madeira flora is now in the press, and his large collection of island plants and grasses has been presented to the new museum at Funchal.

Dr. EDWARD GAVED STOCKER, who died on April 28th at Grampound-road, Cornwall, was the son of Thomas Stocker of St. Austell, and born there in 1862. He was educated at Caversham and University College and at St. Bartholomew's Hospital, where he won an open scholarship in science. After holding house appointments at the West London Hospital he settled in practice at Clevedon, becoming medical officer to the hospital there and surgeon-captain to the 2nd Wessex Field Company, R.E. In the late war he first served with a Wessex division of engineers, and later was in medical charge of Wiltshire military hospitals, ending up as embarkation medical officer at Plymouth. Dr. Stocker had many interests in the west country, its history and welfare, and his favourite recreations were hunting, motoring, and golf.

Lieut.-Colonel HERBERT JAMES WALTON, I.M.S. (retd.), qualified from St. Bartholomew's Hospital in 1893, going on to take the highest honours at London University. At Netley he gained the first Montefiore prize for military surgery and the Martin medal for military medicine. Entering the Indian Medical Service in July, 1896, he was in military employ until 1905, when he became civil surgeon, United Provinces. Meanwhile his war services had brought him medals for the Frontier of India (1897–98), China (1900), and Tibet (1903–04). In 1913–14 he held the chair of pathology at King George's Medical College, Lucknow, reverting to military duty in April, 1915. He died at Godalming on May 4th.

PANEL AND CONTRACT PRACTICE

Post-graduate Study

FORTY-ONE insurance practitioners have now completed refresher courses at the Royal Northern Hospital, London, and at the University of Leeds under the Ministry of Health's scheme. Courses for a further 40 doctors are in progress at Liverpool University and at the Nottingham General Hospital and 61 doctors began similar courses on Monday last at the University of Birmingham and at the British Post-graduate Medical School, Hammersmith, where a continuous series of courses is being provided. Bristol, Cambridge, Newcastle, Oxford, and Sheffield will also take part. By arrangement with the Department of Health for Scotland 35 English doctors will take courses at Scottish centres and a corresponding number of Scottish doctors at Hammersmith. In all about 850 English insurance practitioners will take part this year.

Lavish Prescribing

Two partners had their prescribing for the first quarter of 1937 investigated by the panel committee, at the instance of the Ministry of Health. The committee came to the conclusion that the practitioners' prescribing showed evidence of excess, estimated (after making every possible allowance) at not less than £25. The practitioners appealed to the Ministry against this decision but their appeal was dismissed. During the period under review the two partners issued 7217 prescriptions to 1420 patients, the mean number of patients on their lists being 2886. The average cost per person and the average number of prescriptions per person were 74 per cent. and 67 per cent. respectively above the areal averages. The total cost of the 7217 prescriptions was £248 0*s.* 8*d.*; on the areal average it would have been £141 17*s.* 11*d.* The senior partner appeared, to represent both doctors. The report of the appeal tribunal says that his attitude to the whole proceedings seemed one of polite tolerance; he seemed reluctant to consider any question of economy. The chief factors leading to the high charge on the drug fund were frequency of administration and frequency of prescribing.

Both partners showed a bias towards ordering medicine every four hours, 56 per cent. of the mixtures bearing this signature. The frequency of this instruction for the whole of England all the year round is 14 per cent. Naturally, however, the ratio is greater in the winter than in the summer months because of the prevalence of respiratory catarrhs. To test the frequency of prescribing comparable figures were put in from four neighbouring practices, two of which were admitted by the senior partner to be comparable with his own. In these two practices 48 per cent. of the panel list were prescribed for during this quarter, a figure only just below that of the practice concerned (49 per cent.). The number of prescriptions issued per patient, however, was only 4·01 as against 5·08 in this case (the mean for the whole county was 3·61). The senior partner took exception to the fact that each prescription on a form was counted as a unit, but as this method was applied to the controls the objection was held to be invalid. The number of prescriptions per person on the prescribing list was 2·15 in comparison with 1·92 for his neighbours. Of the total number of scripts 65 per cent. contained more than one prescription, as compared with a mean for the whole country of 25 per cent. The report continues:

A study of the actual scripts reveals a certain lavishness of prescribing irrespective of the time elapsing between consecutive prescriptions. The use of proprietary articles accounted for 15·96 per cent. of the total ingredient cost as compared with 4·5 per cent. for England as a whole. Elastoplast bandages for five patients (47 bandages) cost £5 17*s.* 6*d.*, a figure which seemed inexplicable till the senior partner told us that his habit was to replace the bandage every week over considerable periods. The same patients at the same time were given a large amount of lotions and dressings (generally half a pound of plain lint). In the opinion of the referees such frequent changes are quite unnecessary, and detract from the efficiency of the treatment whether considered from practical or theoretical grounds.

The insurance committee decided to recommend the Minister to withhold £25 from the practitioners' remuneration.

Dr. J. C. W. Methven has been appointed a commissioner of prisons in the place of Dr. W. Norwood East, who is retiring.

PARLIAMENTARY INTELLIGENCE

NOTES ON CURRENT TOPICS

Local Authorities and the Blind

IN the House of Commons on May 6th, when the Prevention and Treatment of Blindness (Scotland) Bill was read a third time and passed,

Mr. ALLAN CHAPMAN moved an amendment providing that any scheme submitted by a local authority should be subject to the approval of the Department for Health for Scotland. The purpose of this was to ensure that any conditions the authority laid down which might be considered inexpedient were eliminated at the source and before the scheme came into operation. In seconding the amendment,

Mr. GARRO-JONES said that the Bill entitled local authorities to take such measures as they thought would assist in the prevention of blindness. It had been pointed out that those words did not mean what they said, but this argument had been brought to nought by evidence that some local authorities acting in advance of the statute had interpreted the provisions in the Bill as much wider than they were intended to be, and had, in fact, sought to bring pressure, or at any rate invested themselves with power to bring pressure, upon blind persons in order to prevent their marriage if the medical officer of health thought it would be undesirable. In view of this evidence an undertaking had been given that the matter would be brought within the purview of the Secretary of State for Scotland.

Better Rural Housing

The support of county medical officers of health for the rural housing Acts was expressed by Sir Francis Fremantle during the debate on the second reading of the Housing (Rural Workers) Amendment Bill on May 9th. Sir Kingsley Wood had said he would ask district councils to ascertain themselves what cottages needed reconditioning, and where the owners were unwilling to do the work, to consider exercising their powers to buy the cottages and themselves recondition them. Sir Francis thought there was a danger that local authorities might make grants for keeping alive and reconditioning houses which were not worthy to be reconditioned. The county medical officers of health, through their association, were, he said, strongly in favour of this Bill, but they were anxious that much more control should be exercised. The M.O.H. for Devon had reported well of the working of the Acts in his county. There were many good houses, built in the middle of the last century, which were quite capable of being improved.

Insanity and Marriage

During the second-reading debate on the Administration of Justice (Miscellaneous Provisions) Bill, which has passed through the House of Lords, Mr. A. P. HERBERT referred to the position of doctors when certifying insanity in connexion with matrimonial causes. Complaint was being made that in the administration of the Matrimonial Causes Act passed last year the intentions of Parliament were not being carried out. The first point was with regard to the provision which gave a right to sue for a dissolution of marriage where the co-respondent had been of unsound mind for five years. During debate last year a great deal was heard about the possibility of a doctor being able to say that a person was incurably insane. But now the British Medical Association had raised two new points. Their council had considered the ethical position of the medical man, in charge of an insane patient, approached for an opinion by a prospective petitioner; they were advised that any opinion as to the patient being of unsound mind would not be covered by the protection given under the Mental Treatment Act or the Lunacy Act; and that the safest course would be for the practitioner to decline to express any opinion save by direction of the court, although he might place his records at the disposal of an independent medical expert nominated by the petitioner. The B.M.A. council considered that the medical man responsible for the care of the patient would not be justified in giving an opinion except at the express direction of the court. The adoption of this attitude would, however, make the Act unworkable. Mr. Herbert's other point was that there were many cases in which husband or wife had been deserted and the magistrate had inserted in the separation order what was called a non-cohabitation clause, with the result that they were not entitled to divorces. He thought the law officers should look into this.

In the House of Commons on May 3rd the Nursing Homes Registration (Scotland) Bill was read a second time.

QUESTION TIME

WEDNESDAY, MAY 4TH

Silicosis Certificates

Mr. ELLIS SMITH asked the Home Secretary the number of applications for certificates from people claiming to be suffering from silicosis; the number granted; the number of applications made for certificates claiming that death was due to silicosis; and the number of certificates granted in the North Staffordshire area of the pottery industry, with separate particulars for each year 1925 to 1938, respectively.—Mr. GEOFFREY LLOYD, Under-Secretary, Home Office, replied: The following table relates to applications from the Pottery Industry (practically all from North Staffordshire) dealt with by the Stoke Panel of the Silicosis Medical Board since June 1st, 1931. The Board did not previously deal with pottery cases, and I regret that earlier figures are not available.

—	Death certificates.		Disablement certificates.	
	Granted.	Refused.	Granted.	Refused.
June–December 1931 ..	17	12	31	45
1932 ..	31	9	90	71
1933 ..	31	9	67	72
1934 ..	30	5	52	48
1935 ..	31	6	65	61
1936 ..	30	6	24	49
1937 ..	42	6	38	47

THURSDAY, MAY 5TH

Lead Poisoning

Mr. HOLLINS asked the Home Secretary whether he was aware that the effect of lead poisoning might not become evident until some years after a worker, who had been employed in a lead process, had left his occupation; and whether he would consider extending the period in which a claim for compensation could be made after a worker had ceased to be employed in a lead process from one year to at least five years or to eliminate the time limit. —Sir SAMUEL HOARE replied: The point will be noted for consideration when an opportunity occurs for amending legislation, and if the hon. Member will send me particulars of any cases he has in mind I shall be glad to consider them.

Chronic Invalids and Voting Facilities

Rear-Admiral BEAMISH asked the Home Secretary whether he would make arrangements whereby facilities might be afforded to chronic invalids to record their votes at parliamentary elections on lines similar to those accorded to absent voters.—Sir SAMUEL HOARE replied: Legislation would be necessary to give effect to my hon. friend's proposal. The proposal is not free from difficulty, but it has been noted for consideration when opportunity arises.—Rear-Admiral BEAMISH: Does the right hon. gentleman realise that such a concession would be a great boon to a large number of intelligent citizens? Is it not a principle which already obtains in this House in regard to recording votes of hon. Members who are

blind, or who are chronic invalids?—Sir S. HOARE: That may be so, but this proposal administratively is not free from difficulty. It will be kept in mind in any legislation dealing with the subject.

Cesspools and Public Health

Mr. LIDDALL asked the Minister of Health whether he was aware that the provisions of Section 37 of the Public Health Act, 1936, perpetuated the system of cesspools by withholding from a local authority the power to reject building plans of dwelling-houses on unsewered land solely on account of proposed cesspools; and whether he would consider providing regulations to prohibit the building of cesspools for any dwelling-house within an urban district.—Sir KINGSLEY WOOD replied: The Public Health Act, 1936, gives, I am advised, ample powers to local authorities to secure the proper construction and maintenance of cesspools and to prevent their being a nuisance or prejudicial to health.—Mr. LIDDALL: Does not my right hon. friend consider that the Public Health Act should give local authorities the power to reject plans solely on the ground of the provisions of a cesspool? Does he consider that in 1938 it is right that dwelling-houses in urban districts should have cesspools?—Sir K. WOOD: I think this would be a very difficult proposition to accept.

MONDAY, MAY 9TH

Milk Schemes

Mr. RIDLEY asked the Minister of Agriculture what had been the increased consumption of milk in the families participating in the special milk schemes in the areas in which they were at present operating.—Mr. MORRISON replied: I am informed by the Milk Marketing Board that there has been an average increase of 0·13 pint, or 61 per cent., in the daily per capita consumption of milk in families participating in the experimental schemes for the supply of cheap milk to nursing mothers and children under five years of age in the Special Areas.

Maternal Welfare

Miss WARD asked the Minister of Health how many local authorities in the Special Areas failed to provide, where necessary, additional nourishment to expectant mothers at all stages of pregnancy.—Sir KINGSLEY WOOD replied: All the 35 authorities responsible for maternity and child welfare services in the Special Areas supply additional nourishment in the form of milk to expectant mothers, and all but 5 of them do so at all stages of pregnancy. 22 of the 35 authorities supply other forms of additional nourishment to mothers, the great majority at all stages of pregnancy. In addition the scheme introduced by the National Birthday Trust Fund for providing other additional food for certain groups of expectant mothers is in operation in most of the Special Areas.

Nursing Services Committee

Sir ARNOLD WILSON asked the Minister of Health whether the decision not to print the minutes of evidence of the Departmental Committee on Nursing was taken by the chairman of the committee or on instructions from the Treasury, and on what grounds.—Sir KINGSLEY WOOD replied: No decision has yet been taken as to the publication of the evidence given before this committee.

Ventilation of the House

Mr. DAY asked the First Commissioner of Works whether, in view of the repeated representations that his department has received in the past to the effect that the existing system of ventilation in the Chamber was prejudicial to health, he would now undertake to have the necessary alterations made for the improvement of the same.—Sir P. SASSOON said that although admittedly the present system left something to be desired from the point of view of comfort during the summer months, the results of exhaustive study of the conditions in the Chamber, together with the advice which he had received from various expert authorities, pointed to the conclusion that the conditions were in no way prejudicial to health. Much careful study had been given to an improved ventilation scheme, but in view of the heavy demands at present being made by the defence programme on the engineering industry it was desirable to keep this scheme and others of a comparable character in reserve for consideration when the peak of the armament programme had been passed and when it would be both more advantageous and more opportune for the industry to have ordinary civil works available for execution.—Mr. CROSSLEY: What can this really have to do with rearmament? Why should Members be kept for years longer in a thoroughly lethargic and dull atmosphere?

Prison Officers' Sick Leave

Mr. GRAHAM WHITE asked the Secretary of State for the Home Department if he would indicate the average number of days sick leave taken by prison officers, principal officers, and chief officers in His Majesty's prisons during the last 12 months for which statistics were available; and if he would further indicate the maladies from which officers of these grades most frequently suffered, as disclosed by returns in the possession of his department.—Sir SAMUEL HOARE replied: The average number of days sick leave taken by prison officers during the year 1937 is as follows:—

Men.		Women.	
Officers	9·2	Officers	10·0
Principal officers	7·6	Principal officers	9·6
Chief officers	5·2	Matrons	4·4
Foremen of works and engineers	4·0	Chief officers	10·0
	8·7		9·6

I regret that the information asked for in the last part of the question is not available and could not be obtained without an unjustifiable expenditure of time and money.

Diphtheria Deaths

Sir ARNOLD WILSON asked the Minister of Health the total number of deaths from diphtheria in England and Wales between the ages of 0–15 for each of the years 1933 to 1936, and the death-rate per thousand children living between those ages.—Sir KINGSLEY WOOD replied: The following is the information desired:—

—	Diphtheria—England and Wales.	
	Deaths of children under 15 years of age.	Death-rate per 1000 children living under 15 years of age.
1933 ..	2487	0·261
1934 ..	3826	0·402
1935 ..	3256	0·351
1936 ..	2884	0·318

Purity Standard for Jam

Mr. BANFIELD asked the Minister of Health whether he was aware that there was no legal standard of content and purity for jam; that recently public analysts of Birmingham, Leicester, and in Lancashire had commented adversely upon the existing situation; and that adulteration and misdescription was common throughout the country; and whether he would consider introducing legislation to establish the standard for jam agreed upon between the Food Manufacturers Association and the Society of Public Analysts.—Sir KINGSLEY WOOD replied: I would refer the hon. Member to Clause 81 (c) of the Food and Drugs Bill at present before Parliament under which it is proposed to enable regulations to be made dealing amongst other things with the matter in question.

Incident at Birmingham Mental Home

Mr. RHYS DAVIES asked the Minister of Health whether his attention had been drawn to the case of a Birmingham mental home in which two drunken attendants were fined for attacking and beating an inmate while a third stood by and encouraged them; and whether he would called for a report on the conduct of that institution.—Sir KINGSLEY WOOD replied: Yes, Sir, the prosecution in this case was instituted at the instance of the Board of Control, the persons in question having previously been instantly dismissed. I have had before me a report made by two Commissioners of the Board who inspected the

Institution on March 23rd and 24th. They reported favourably upon its administration and upon the care and treatment of the patients.

Bombing of League Anti-epidemic Unit

Mr. NOEL-BAKER asked the Prime Minister if he could make a statement concerning the recent bombing of a League of Nations hospital by Japanese aircraft.—Mr. BUTLER, Under-Secretary for Foreign Affairs, replied: I understand that during a Japanese air raid on Hankow on April 29th the Hankow branch of the League's English-speaking anti-epidemic unit was destroyed, and that two of the Chinese members of the unit were killed.

Milk Schemes in Special Areas

Mr. RIDLEY asked the Minister of Agriculture (1) whether it was proposed to extend the special milk schemes for mothers and children under five years of age to areas other than those in which they were at present operating, and (2) whether it was proposed to extend the special milk schemes now operating in the Rhondda, Jarrow, and other similar areas, beyond the date at present fixed for their termination.—Mr. MORRISON replied: I understand that the Milk Marketing Board do not, at present, contemplate any extension of their experimental schemes in the Special Areas, but as was stated in the White Paper on Milk Policy, the Government propose to bring forward proposals for securing, in coöperation with the industry, a reduction in the price of liquid milk to local authorities generally for the purpose of their maternity and child welfare arrangements.

Mr. RIDLEY asked the Minister of Agriculture what proportion of those entitled to participate in the various special milk schemes at present operating in the Rhondda, Jarrow, and other similar areas, had availed themselves of them.—Mr. MORRISON replied: I am informed by the Milk Marketing Board that, of the persons eligible to participate in the four experimental schemes for the supply of cheap milk to nursing mothers and children under five years of age in the Special Areas, the proportions that have availed themselves of the facilities vary between 60 per cent. in Jarrow and 65 per cent. in Whitehaven.

MEDICAL NEWS

Research in Tropical Medicine

The Medical Research Council, advised by their tropical medical research committee which was appointed after consultation with the Colonial Office, have decided to offer three junior fellowships to medical men who wish to receive training for research work in tropical medicine. Preference will be given to candidates who have already had preliminary experience of methods of research in some branch of medical science. Subject to satisfactory reports, the fellowships will be tenable for three years. The first year will be spent at a school of tropical medicine; the second in doing research in the same or some other institution at home; and the third largely in work under direction at some centre in the tropics. The stipend will be at the rates of £300, £400, and £500 per annum in the successive years, with an additional allowance during service abroad and necessary expenses. In three years' time at least one senior fellowship will be available for candidates who have held the junior fellowships mentioned above. This will be awarded for a further period of three years, carrying stipend at the rate of £600–£750 per annum, with an additional allowance during service abroad and expenses. The time will be spent mainly in research work in the tropics. The council are also prepared to consider immediate applications for senior fellowships from candidates who have had adequate experience in research work, whether already specially trained in tropical medicine or not.

The council further intend to establish in due course, as suitable investigators become available as the result of the fellowship scheme, permanent and pensionable appointment for research work in tropical medicine, including senior posts. Members of this research staff will work partly in the tropics and partly in institutions at home to which they will be attached. The exact terms of service are still undecided, but they will be not less favourable than those which apply to other Government appointments at home or overseas for men of similar professional standing. Inquiries may be addressed to the secretary of the Tropical Medical Research Committee, 38, Old Queen-street, London, S.W.1, with whom applications should be lodged not later than June 16th.

Plastic Surgery Congress

An International Plastic Surgery Congress will be held at the Sarfatti Institute in Milan from Sept. 25th to 27th.

Physical Fitness in Prague

Sokols, members of Czechoslovakia's national athletic organisation, will hold their tenth six-yearly "slet" or assembly in Prague during July. The association, which is voluntary, was started in 1862 and is organised in 3265 local sections. It owns over a thousand gymnasiums and over 2100 playing-fields. It is expected that 120,000 athletes will take part in this year's display. Arrangements to attend the meeting can be made through Messrs. Thos. Cook and Son, Berkeley-street, London, W.1.

University of London

Prof. W. Girling Ball and Dr. A. M. H. Gray have been reappointed to the senate as representatives of the faculty of medicine, and Prof. L. S. Dudgeon as representative of the general medical schools.

University of Birmingham

Among those on whom the university will confer the honorary degree of LL.D. on July 2nd are Dr. Robert Hutchison, P.R.C.P., Sir Cuthbert Wallace, P.R.C.S., and Sir Edward Mellanby, F.R.S. The degrees are being conferred to mark the completion of the Hospitals Centre and the new medical school which is being opened by the King and Queen on July 14th.

An intensive course in industrial hygiene and medicine will be held at this university from Sept. 12th to 23rd. The syllabus includes the following subjects: non-occupational diseases in industry; factory ventilation, lighting, and sanitation; industrial skin diseases; lead poisoning in modern industry; the metallic poisonings; organic toxins and solvents; the dust diseases; industrial eye diseases; fatigue and practical psychology in the factory; mine fumes, safety appliances, and rescue work; the organisation of a works medical service; and medico-legal problems. Further information may be had from Dr. H. E. Collier, the department of industrial hygiene and medicine, the University, Edmund-street, Birmingham.

Royal Medico-Psychological Association

The annual meeting of this association will be held at Ilkley, Yorkshire, on July 6th, 7th, and 8th.

Kathleen Schlesinger Research Fellowship

The Medical Research Council have appointed Dr. Karl Stern to this fellowship for the year 1938-39. It is provided from a fund established by the late Mr. Eugen M. Schlesinger and Mrs. Schlesinger in memory of their daughter: it is given for investigations of cysts of the brain or allied conditions, and is ordinarily tenable at the National Hospital for Diseases of the Nervous System, Queen-square, London.

St. Mark's Hospital, London

On May 5th the Princess Royal visited this hospital to open the nurses' home, which is the first stage in an extension scheme. The Lord Mayor, president of the hospital, said that the home had been built because the hospital committee recognised that everything possible should be done to ensure the comfort and well-being of those who ministered to the patients. The home provided a separate bedroom for each nurse, three sitting-rooms, a large recreation room overlooking the garden court, and a room in which nurses can entertain their visitors. When the hospital began its work in 1835 the total number of patients was only 131; in 1937 there were 1003 in-patients and 11,000 out-patients. Approximately £25,000 was still required to cover the cost of the nurses' home and the reconstruction and extensions now to be put in hand.

Royal Statistical Society

A meeting of this society will be held in the hall of the Royal Society of Arts, John-street, Adelphi, London, W.C., at 5.15 P.M. on Tuesday, May 17th, when Dr. Percy Stocks will read a paper on the effects of occupation and of its accompanying environment on mortality.

West London Medico-Chirurgical Society

Sir William Willcox will deliver the Cavendish lecture to this society on Wednesday, June 1st, at 8.30 P.M., at Kensington town hall. He will speak on toxicology with reference to its criminal aspects. The annual conversazione and medical and surgical exhibition will take place after the lecture.

Royal Medical Benevolent Fund

At a recent meeting of the committee three annuitants were elected, and thirty-eight beneficiaries were awarded grants. Eleven of these were new applicants. The following are particulars of three cases:—

Widow, aged 64, of M.R.C.S. who died in 1916 at the age of 42. The widow has had a salaried post in social work for many years but owing to the closing down of the association lost her employment in December, 1937, and now finds it impossible to get fresh employment. Her two children, aged 34 and 30, are unable to contribute to her support. Fund voted an allowance at the rate of £1 a week for six months and is seeking the coöperation of other charitable societies.

Daughter, aged 60, of M.R.C.S. who in died 1914 at the age of 76. The daughter has helped her mother to run a boarding-house since 1914 and they have just managed to maintain themselves. The mother is now 83 and all work falls on the daughter who does the cooking as well as looking after her mother. For years she has had a hard life and a struggle to make two ends meet, with no money for extras or a holiday. Fund voted £20 to enable the daughter to have a holiday and rest.

Widow, aged 66, of L.S.A. who died in 1915 at the age of 52. Has invalid daughter aged 32. The widow supported herself and educated her daughter by successfully running a boarding-house until 1933, when circumstances forced her to give up. Recently she has suffered from a duodenal ulcer which has necessitated nursing-home treatment. Her own and her daughter's illnesses have been a great drain on her resources and the money which she had put aside has been used up. Only income now £60—invalid daughter is able to earn a little by teaching painting £26 per annum. Fund voted an allowance at the rate of £1 a week for six months, when the case will be reviewed.

New annual subscribers are urgently needed by the fund. Cheques may be sent to the hon. treasurer of the fund, 11, Chandos-street, London, W.1.

Medical Diary

May 16th to May 22nd

SOCIETIES

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.
TUESDAY.
5 P.M., meeting of fellows.
THURSDAY.
Dermatology. 5 P.M. (cases at 4 P.M.), annual general meeting. Dr. H. MacCormac: (1–2) Atrophic Lichen Planus in Women. Dr. H. Semon: (3) Benign Lymphogranulomatosis (Schaumann). Dr. Sydney Thomson: (4) Congenital Cutis Verticis Gyrata. (5) Leiomyomas. Dr. A. M. H. Gray: (6) Sarcoma of the Skin. (7) Urticaria Pigmentosa. (8) Acneiform Lesions in a Child. Dr. Godfrey Bamber: (9) Rosaceous Tuberculide.
Neurology. 9 P.M., annual general meeting. Prof. Georges Guillain (Paris): "Le syndrome myoclonique rythmé vélo-pharyngo-oculo-diaphragmatique."
FRIDAY.
Obstetrics and Gynæcology. 8 P.M., annual general meeting. Mr. Victor Bonney: Erythroblastosis Fœtalis; and Leucoplakic Vulvitis and the States that Mimic It. Mr. Kenneth Walker and Mr. B. P. Wiesner, Ph.D.: Male Sterility and the Assessment of Male Fertility. Mr. James Wyatt: Femoral Thrombosis.
Radiology. 7 P.M., annual general meeting.

ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION.
FRIDAY.—2.30 P.M. (11, Chandos-street, W.), discussion on the Alleged Inadequacy in Numbers of Medical Officers in Mental Hospitals.
Pathological, Bacteriological and Biochemical Subcommittee.
THURSDAY.—8 P.M. (Central Pathological Laboratory, Denmark-hill, S.E.), Dr. D. N. Parfitt: The Uses of T.A.B. Vaccine in Psychiatry. Dr. W. M. Ford-Robertson: Leucocyte Activity in the Manic-depressive Psychosis.

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck-street, W.
THURSDAY.—6.30 P.M., annual general meeting.

Medical Meeting,
FRIDAY.—11 A.M., visits to the British Red Cross Society's Clinic for Rheumatism, Peto-place, N.W. 5.30 P.M., case demonstration and discussion.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, Manson House, 26, Portland-place, W.
THURSDAY.—8.15 P.M., Dr. P. C. C. Garnham: The Placenta in Malaria with special reference to Reticulo-endothelial Immunity. Major H. W. Mulligan will open the discussion.

TUBERCULOSIS ASSOCIATION.
FRIDAY.—5.15 P.M. (26, Portland-place, W.), Dr. J. Browning Alexander, and Dr. G. J. Johnston and Mr. C. A. Collingwood: Trauma and Tuberculosis. 8.15 P.M., Dr. J. T. Hunter and Mr. J. B. Hunter: Anæsthetics in Thoracic Surgery.

SOCIETY OF RADIOTHERAPISTS OF GREAT BRITAIN AND IRELAND.
FRIDAY.—5 P.M. (Middlesex Hospital, W.), Prof. Hugh Cairns, Mrs. E. L. G. Hilton, and Dr. Robert McWhirter: Radiotherapy of Brain Tumours.

NORTH LONDON MEDICAL AND CHIRURGICAL SOCIETY.
FRIDAY.—9.15 P.M. (Royal Northern Hospital, Holloway-road, N.), Dr. James Maxwell: Acute Infections of the Lung. (Presidential address.)

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

BRITISH POSTGRADUATE MEDICAL SCHOOL, Ducane-road, W.
TUESDAY.—4.30 P.M., Dr. Gardiner-Hill: Diseases of the Ductless Glands.
WEDNESDAY.—Noon, clinical and pathological conference (medical). 2 P.M., Mr. E. J. King, Ph.D.: Acid-base Metabolism. 3 P.M., clinical and pathological conference (surgical).
THURSDAY.—2.15 P.M., Dr. Duncan White: radiological demonstration. 3.30 P.M., Mr. Aleck Bourne: Salpingitis.
FRIDAY.—2 P.M., clinical and pathological conference (obstetrics and gynæcology).
Daily, 10 A.M. to 4 P.M., medical clinics, surgical clinics and operations, obstetrical and gynæcological clinics and operations.

ST. GEORGE'S HOSPITAL, S.W.
THURSDAY.—5 P.M., Dr. A. J. Lewis: Psychiatric demonstration.

LONDON SCHOOL OF DERMATOLOGY, 5, Lisle-street, W.C.
MONDAY.—5 P.M., Dr. H. MacCormac: Treatment of Syphilis.
TUESDAY.—5 P.M., Dr. Mitchell Heggs: Skin Affections of the Hands and Feet.
WEDNESDAY.—5 P.M., Dr. I. Muende: Pathological Demonstration.
FRIDAY.—5 P.M., Dr. L. Forman: Alopecia.

HOSPITAL FOR SICK CHILDREN, Great Ormond-street, W.C.
THURSDAY.—2 P.M., Mr. Denis Browne: Treatment of Empyema. 3 P.M., Dr. D. G. Edwards: When Does a Blood Count Aid Diagnosis?
Out-patient clinics daily at 10 A.M. and ward visits at 2 P.M.

ST. MARY'S HOSPITAL, W.
TUESDAY.—5 P.M. (Institute of Pathology and Research), Prof. John Mellanby, F.R.S.: Bile Salts as the Dominant Factor in Intestinal Secretions and Digestion.

NATIONAL HOSPITAL FOR DISEASES OF THE HEART, Westmoreland-street, W.
TUESDAY.—5.30 P.M., Dr. D. Evan Bedford: Hypertensive Heart Disease.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, W.
MONDAY to SUNDAY.—BROMPTON HOSPITAL, S.W., all-day course in thoracic surgery.—ST. JOHN CLINIC AND INSTITUTE OF PHYSICAL MEDICINE, Ranelagh-road, S.W., Sat. and Sun. course in physical medicine.—MAUDSLEY HOSPITAL, Denmark-hill, S.E., afternoon course in psychological medicine.—ST. JOHN'S HOSPITAL, 5, Lisle-street, W.C., afternoon course in dermatology. (Open to non-members.)

MANCHESTER ROYAL INFIRMARY.
FRIDAY.—4.15 P.M., Dr. Charles Don: clinical demonstration.

Vacancies

For further information refer to the advertisement columns

Accrington, Victoria Hosp.—H.S., £175.
Barking Borough.—Asst. M.O., £600.
Birmingham City, Mental Hosp. Dept.—Jun. Asst. M.O., £350.
Birmingham, Queen's Hosp.—Res. Surg. Reg., £125.
Birmingham and Midland Eye Hosp.—H.S., at rate of £130.
Blackburn County Borough.—Asst. M.O.H. and Asst. School M.O., £600.
Bolton Education Committee.—Asst. M.O.H. and Asst. School M.O., £500.
Bolton Royal Infirmary.—Asst. Res. Surg. O. and H.P., each at rate of £200. Also three H.S.'s, each £150.
Boston General Hosp.—Res. M.O., at rate of £150.
Brighton, Royal Sussex County Hosp.—H.P., £150.
Bristol, Winford Orthopædic and Heart Hosp.—M.O., £325.
Bury County Borough.—Asst. M.O.H., £500.
Cairo, Memorial Ophthalmic Laboratory.—Pathologist and Bacteriologist, £E.1200.
Canterbury, Kent and Canterbury Hosp.—Hon. Physician.
Cardiff, King Edward VII Welsh National Memorial Association. Asst. Res. M.O. for North Wales Sanatorium, £200.
Central London Throat, Nose, and Ear Hosp., Gray's Inn-road, W.C.—Third Res. H.S., at rate of £75.
Central Middlesex County Hosp., Acton-lane, Willesden, N.W.—Pathologist, £1100. Also Res. Asst. M.O., £400.
Chester, Barrowmore Tuberculosis Sanatorium and Settlement.—Jun. Asst. M.O., at rate of £200.
Coventry City.—Asst. School M.O., &c., £500.

Derbyshire County Sanatorium.—Jun. Res. Asst. M.O., £350.
Dreadnought Hosp., Greenwich, S.E.—Receiving Room Officer, at rate of £100.
Edgware, Redhill County Hosp.—Obstetric Surgeon, £500.
Evelina Hosp. for Sick Children, Southwark, S.E.—H.P., at rate of £120.
Gloucestershire County Council.—Two Asst. County M.O.H.'s, each £500.
Gravesend and North Kent Hosp.—Jun. H.S., £120.
Halifax Royal Infirmary.—Second H.S. to Eye, Ear, Nose, and Throat and Medical Depts., at rate of £175.
Hampstead General and North-West London Hosp., Haverstock Hill, N.W.—Res. Cas. Surg. O., at rate of £100.
Harefield, County (Tuberculosis) Sanatorium.—Jun. Res. Asst. M.O., at rate of £250.
Hastings, Royal East Sussex Hosp.—Asst. Pathologist, £300. Also Hon. Surgeon.
Hertford County Hosp.—H.S., at rate of £200.
Heston and Isleworth Borough.—M.O.H. and School M.O., £1000. Also Asst. M.O.H. and School M.O., £500.
His Majesty's Colonial Service.—Bacteriologist for Veterinary Dept. in Kenya, £500.
Home Office.—Three Medical Inspectors of Factories, each £750.
Hornsey Central Hosp., Park-road, N.—Hon. Radiologist.
Hosp. for Consumption, &c., Brompton, S.W.—Res. M.O., £350.
Hosp. for Sick Children, Great Ormond-street, W.C.—Asst. Res. Surg. O., £100. Also two Res. H.P.'s and Res. H.S., each at rate of £50.
Huddersfield Royal Infirmary.—H.S. to Eye, Ear, Nose, and Throat Depts., at rate of £150.
Hull City Hosp. for Infectious Diseases, Cottingham.—Res. M.O., £350.
Hull Royal Infirmary.—Second Cas. O., at rate of £150.
Hull and Sculcoates Dispensary.—Res. M.O., £550.
Infants Hosp., Vincent-square, S.W.—Hon. Surgeon. Also Clin. Assts. to Out-patient Dept.
Ipswich Isolation Hosp.—Asst. M.O.H., &c., £450.
Isleworth, West Middlesex County Hosp.—Asst. M.O., £400.
Kettering and District General Hosp.—H.P., £150.
Lancashire Mental Deficiency Acts Committee.—Additional Asst. M.O., £550.
Lancaster Royal Infirmary.—H.S., at rate of £130.
Leeds City.—Asst. M.O. for Maternity and Child Welfare, £500.
Leicester Royal Infirmary.—Res. Radiologist, at rate of £200.
Lincoln County Hosp.—Jun. H.S., at rate of £150.
Liverpool Convalescent Home, Woolton.—Lady Supt.
Liverpool Heart Hosp.—H.P., at rate of £100.
Liverpool Hosp. for Consumption and Diseases of the Chest.—Med. Supt. for Delamere Sanatorium, £800.
London County Council.—First Asst. M.O., £750. Asst. M.O.'s, Grade I, £350. Asst. District M.O.'s, £280 and £125. Consultant and Specialist Services: Part-time Ear, Nose, and Throat Specialist, £200. Also Organiser of School Meals, £300.
London Homœopathic Hosp., Great Ormond-street, W.C.—Res. H.P., Res. H.S., and Res. Med. and Cas. O., each at rate of £100. Also Two Hon. Clin. Assts. for Manipulative Surgery.
London Jewish Hosp., Stepney Green, E.—Res. M.O., and H.P., each at rate of £150. Also H.S. and Cas. O., each at rate of £100.
London University, King's College.—Demonstrator in Physiology, £100 per term.
Maidstone, West Kent General Hosp.—H.S., £175.
Manchester, Ancoats Hosp.—Orthopædic Registrar, £50.
Manchester Royal Children's Hosp.—Res. M.O., at rate of £150.
Manchester Royal Eye Hosp.—Out-patient M.O., £200.
Manchester Royal Infirmary.—Res. Jun. M.O. for Barnes Convalescent Hosp., at rate of £150.
Manchester, St. Mary's Hosps.—Res. Obstet. Officer, £150. Also two H.S.'s, each at rate of £50.
Manchester University.—Asst. Lecturer in Chemical Pathology, £400.
Marie Curie Hosp., 2, Fitzjohn's-avenue, N.W.—Res. M.O., £100.
Metropolitan Hosp., Kingsland-road, E.—Cas. O. and Res. Anæsthetist, £100.
Miller General Hosp., Greenwich-road, S.E.—Cas. O. and H.S., at rate of £150 and £100 respectively.
North Middlesex County Hosp., Silver-street, N.—Jun. Res. Asst. M.O., at rate of £250.
Norwich, Norfolk and Norwich Hosp.—H.P., £120.
Nottingham General Dispensary.—Res. M.O., £300.
Nottingham General Hosp.—H.P., at rate of £150.
Oldham, Municipal Hosp.—Res. Asst. M.O., at rate of £200.
Oswestry, Robert Jones and Agnes Hunt Orthopædic Hosp.—H.S., at rate of £200.
Oxford, Radcliffe Infirmary.—Hon. Physician to Dept. of Physical Medicine.
Plymouth, Prince of Wales's Hosp., Greenbank-road.—Res. Surg. O., at rate of £225.
Prison Commission, Home Office, S.W.—M.O., Class II, £525.
Public Schools Exploring Society.—Hon. Surgeon.
Queen Mary's Hosp. for the East End, Stratford, E.—Appointments, £150–£120.
Reading, Royal Berkshire Hosp.—Asst. Hon. Surgeon.
Royal College of Surgeons of England.—Examiner in Dental Surgery.
Royal Free Hosp., Gray's Inn-road, W.C.—Res. Cas. O., £150. Also In-patient Obstet. Asst. and Second H.P.
Royal Naval Medical Service.—Medical Officers.
Royal Northern Hosp., Holloway.—Gynæcologist in V.D. Dept.
Royal Waterloo Hosp. for Children, &c., S.E.—Hon. Asst. Surgeon. Also H.S., at rate of £100.
St. George's Hosp., S.W.—Res. Anæsthetist, at rate of £100.
Salford City.—Asst. M.O. for V.D. Treatment Centre, £500.
Sheffield Royal Infirmary.—Clin. Asst. to Ophth. Dept., £300. Also Ophth. H.S., at rate of £150.
Society for Relief of Widows and Orphans, 11, *Chandos-street, W.*—Officers.
Southampton Borough General Hosp.—Asst. Res. M.O., £350.
Southampton Free Eye Hosp.—H.S., at rate of £150.
Southampton, Royal South Hants and Southampton Hosp.—H.P., Res. Anæsthetist, two H.S.'s, and Cas. O., each at rate of £150.
Southend-on-Sea General Hosp.—Cas. O., at rate of £100.
Southern Rhodesia Medical Service.—Government M.O., £600.
Stoke-on-Trent, Burslem, Haywood, and Tunstall War Memorial Hosp.—Res. H.S., at rate of £175.
Uxbridge, Hillingdon County Hosp.—Res. Cas. M.O., at rate of £350.
Virginia Water, Holloway Sanatorium.—Jun. Asst. M.O., £350.
West Bromwich, Hallam Hosp.—H.P., at rate of £200.
West End Hosp. for Nervous Diseases, Gloucester-gate, N.W.—Res. H.P., £125.
West London Hosp., Hammersmith-road, W.—Additional Hon. Reg. for Throat, Nose, and Ear Dept. Also Hon. Clin. Asst. in X Ray (Diagnostic) Dept.
Willesden General Hosp., Harlesden-road, N.W.—Biochemist, at rate of £100.
Windsor, King Edward VII Hosp.—Cas. O., £120.
Wolverhampton Royal Hosp.—Res. Asst. Path. and Res. M.O., £150.
Woolwich and District War Memorial Hosp., Shooters Hill, S.E.—H.P., at rate of £100.
York County Hosp.—Res. Anæsthetist and Second H.S., £150.
York Dispensary.—Two Res. M.O.'s, each £175.
The Chief Inspector of Factories announces vacancies for Certifying Factory Surgeons at Bridlington (York, E.R.), and Cleland (Lanark).

Births, Marriages, and Deaths

BIRTHS

CAREW-SHAW.—On May 6th, at Bentinck-street, W.1, the wife of Mr. E. Carew-Shaw, F.R.C.S.—a son.
EVANS.—On May 3rd, at D.10, Nuffield House, the wife of Dr. Roy Evans, of Epping—a daughter.
PALMER.—On April 24th, in Shillong, Assam, the wife of Dr. G. W. Palmer—a son.
STARKIE.—On May 1st, at Devonshire-place, W.1, the wife of Dr. E. T. W. Starkie—a daughter.

DEATHS

COOKE.—On May 9th, at Tottenham, Francis Henry Cooke, M.R.C.S. Eng., late of Birch, Colchester, aged 74.
HANCOCK.—On May 6th, at a London nursing-home, George Charles Hancock, C.B.E., M.R.C.S. Eng., D.P.H., Barrister-at-Law, aged 70.
HIND.—On May 3rd, at Twickenham, Henry Joseph Hind, M.R.C.S. Eng., L.S.A. Lond., aged 85.
LIVINGSTONE.—On May 9th, at Richmond, Surrey, John Livingstone, M.D., C.M. Edin., T.D., Major, R.A.M.C. (T.).
PORTER.—On May 5th, at Bristol, George Porter, M.D. Edin.
PRIOR.—On May 7th, Edward Symes Prior, M.R.C.S. Eng., of Hampstead Way, N.W.11.
ROBSON.—On May 5th, Robert Boyd Robson, M.B. Aberd., of Seven Kings, aged 65.
SIMPSON.—On May 9th, at Chichester, Frederick Hampson Simpson, M.D. Durh., of Bognor Regis.
STOCKER.—On April 28th, Edward Gaved Stocker, M.R.C.S. Eng. (Major, T.D.), R.A.M.C.
WALTON.—On May 4th, at Godalming, Lieut.-Colonel H. J. Walton, M.D. Lond., F.R.C.S. Eng., I.M.S. (retd.).

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages, and Deaths.

THE LANCET 100 YEARS AGO

May 12th, 1838, p. 226.

From a leading article.

. . . It is good policy, then, to watch over the health of the Navy: and the seamen have, besides, irrefragable claims on the country, founded on principles of rigorous justice. In time of war they are impressed: the ships are prisons, the captains gaolers; the men are dragged into the service by press-gangs, scourged into obedience by the cat, tied up to the mast, or suspended at the yard-arm, whenever they show the least restiveness under the rein of the greatest despot on the seas. The press-gangs in the late wars supplied the victualling gangs with victims; and foul ships, bad biscuits, putrid beef, raised up mutineers to writhe under the lash, and under a savage captain's eye. The most effectual step in the amelioration of the Royal Navy would be the abolition of Impressment: which would be quite unnecessary if flogging were abolished, the men's health, wants, and comforts attended to, if means of instruction were provided aboard, and the *hope of promotion* were held out to merit among all classes. Men would never undertake voluntarily to eat bad biscuits and bad beef with no hope of ever bettering their condition; but if the circumstances in the Navy were made more inviting than in Merchants' Ships, no dread of fighting, or meeting the foe, would daunt the Mariners of England in War.

NOTES, COMMENTS, AND ABSTRACTS

PROGRESS IN ELECTRO-ENCEPHALOGRAPHY

THE electro-physiology of the cortex has been slow in developing, partly because of the impossibility in many countries of experimenting on the exposed brain of unæsthetised animals. Kornmüller [1] is almost the only experimenter to work systematically without an anæsthetic; his animals were usually curarised, however, and were therefore not strictly normal. His contention that the various cyto-architectonic fields of an animal's brain possess characteristic electrical rhythms or *Eigenströme* has, indeed, been criticised on several grounds, and recently Marinesco, Sager, and Kreindler [2] have described in a short paper some experiments on rabbits which were neither anæsthetised nor curarised. Their results which, as they point out, cannot be directly compared with those obtained either from other animals or in other experimental conditions, suggest that the whole cortex of the rabbit may have a fundamental electrical rhythm of between 2 and 6 per second ". . . associated with the metabolism of the nerve cells." Upon this rhythm are superimposed the discharges characteristic of the several cyto-architectonic and functional fields, of which these authors can recognise three, corresponding roughly with the visual, tactile, and motor areas. The attitude of Marinesco and his colleagues differs from that of Kornmüller, for they consider that "bio-electric differentiation between the various cyto-architectonic fields cannot be made by their characteristic rhythms but only by their functional activities." The very indefiniteness of this statement may be an advance on Kornmüller's rigid dogma of *Eigenströme*.

With the physiological basis still surrounded by the scaffolding of controversy, the structure of clinical electro-encephalography must still be regarded as somewhat speculative, though its fabric grows daily more massive. In an ambitious but not wholly convincing communication Marinesco, Sager, and Kreindler [3] report the results of examination of various pathological conditions. They confirm that the most striking changes in the electro-encephalogram are found when the cerebral cortex is directly affected by such agencies as raised intracranial pressure and cerebral tumours and abscesses, the abnormality consisting usually in the appearance of slow waves. They report abnormalities also in a collection of cases classified symptomatically as "aphasias" and "comas." The usefulness of such a classification is doubtful and the value of the material in this paper is lessened by the technical limitations that prevented the localisation of the discharges. This shortcoming accounts for the difficulty in appreciating the results and opinions of these and several other authors; for, being unable to localise the site of origin of the discharges they observe, they regard most of the features of the pathological electro-encephalogram as modifications of the normal occipital alpha rhythm. The intimate nature of the cerebral potentials may well be the same in health and disease, and there is some justification also for considering the brain as a single functional organ; but on the other hand there is important pragmatic evidence, both from clinical and electro-encephalographic sources, that, particularly in abnormal conditions, one part of the brain may behave independently of the other parts. As an example, in cases of motor aphasia Marinesco and his colleagues found an "alpha rhythm" of from 2·5 to 6 per second. But the records were taken with a single recording system leading from widely spaced electrodes, and the abnormality is just as likely to be due to a typical slow discharge from an abnormal frontal focus (which would fit in more neatly with the clinical picture) as to a slowing of the occipital alpha rhythm. The latter interpretation implies the premise that the alpha rhythm is an expression of the electrical activity of the whole cortex rather than an indication of a state of rest in the visual association areas.

The existence of such important differences in technique and basic ideas makes integration of the results from many laboratories almost impossible, but an excellent review by Fessard [4] presents in a concise and unbiased form the physiological and pathological facts which have been reported in the 82 papers to which he refers. An attempt to summarise this summary might lead to confusion and misunderstanding, but Fessard's conclusions with regard to clinical applications may be noted. Apart from cases of epilepsy and cerebral tumour and abscess (in which its localising power is unequalled) the diagnostic value of electro-encephalography is still only moderate. Its great advantage is that it causes no pain or inconvenience to the patient, and it may be said that when the record shows a distinct abnormality the presence of some organic nervous disease may be deduced, unless of course there are clinical reasons for suspecting the involvement of the nervous system in some general condition such as uræmia. A normal electro-encephalogram by present standards does not, however, exclude the possibility of organic disease; in fact, the clinical limitations of the technique and the precautions which must be taken in interpreting its results are those associated with any method based on empirical correlation.

The absence of an inductive explanation of the phenomena observed and the poverty of physiological data may be ascribed to two main causes—first the difficulty of experimenting with normal animals, and secondly what Adrian has described as the "disappointingly constant" character of the normal rhythms as opposed to the excitingly varied abnormal discharges which have already attracted so many workers from the laboratory to the clinic.

ACUTE NON-SUPPURATIVE THYROIDITIS

OF the inflammatory affections of the thyroid gland, acute non-suppurative inflammation appears to be decidedly the rarest. In *Minerva Medica* (1938, **29**, 353) G. Giordanengo states that since 1904 when the condition was first clearly defined only 54 cases have been published. The earliest sign is the appearance of a tender localised swelling in the thyroid. The swelling does not remain confined to the gland but spreads into the surrounding tissues, and the overlying skin becomes red and œdematous but not adherent. Pain is a prominent symptom, radiating to the ear and arm on the affected side, and the patient assumes a wry-neck attitude. The temperature rises, often to 104° F. Swallowing is painful and difficult, but respiration is rarely impeded.

[1] Kornmüller, A. E., Die bioelektrischen Erscheinungen der Hirnrindenfelder, Leipzig, 1937.

[2] Marinesco, G., Sager, O., and Kreindler, A., *Bull. Acad. Méd., Paris*, 1938, **119**, 360.

[3] — — — *Pr. méd.* April 27th, 1938, p. 650.

[4] Fessard, A., *Paris méd.* April 9th, 1938, p. 301.

After a week or ten days all the symptoms and signs gradually disappear. Diagnosis is usually easy and the prognosis, as regards both life and the function of the thyroid gland, is favourable, though Graves's disease has occasionally followed.

The pathological changes in the gland have been investigated in 9 cases, and are characteristic. The intervesicular tissues show a moderate degree of infiltration with leucocytes or lymphocytes and a few plasma cells, but there is no tendency to abscess-formation, and the process terminates in fibrosis. The vesicles in the affected area show the following changes: first, proliferation of the lining epithelium, followed by detachment and degeneration of the cells; later, progressive disappearance of the colloid, infiltration with polynuclear leucocytes, lymphocytes, and large mononucleated cells; the formation of giant cells; and ultimately transformation of the entire vesicle into fibrous tissue.

The cause of acute thyroiditis is as yet unknown. Bacteriological examination has yielded consistently negative results.

THOMAS STEVENSON

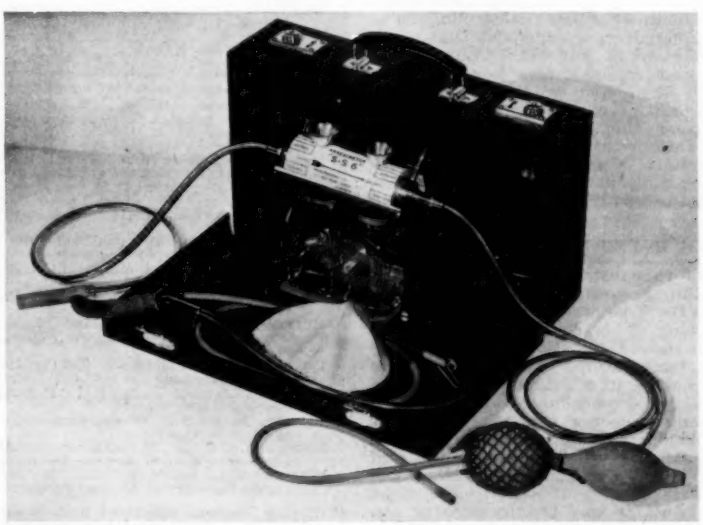
IN a note on the evolution of forensic chemistry, published in our issue of April 16th, we referred to Sir Thomas Stevenson, the analyst and toxicologist. It happens that our note appeared on the very day of Stevenson's birth a hundred years ago, April 14th, 1838. The son of Peter Stevenson, a Yorkshire pioneer in scientific farming, he studied medicine at Guy's Hospital, graduated with distinction in 1863, and set up in practice in Bradford. After a year he returned to Guy's as demonstrator and later lecturer on chemistry, becoming also lecturer on forensic medicine in 1878. Home Office work began to come his way in 1872, and in 1881 he was promoted to the rank of senior scientific analyst. As a witness he was impressive; his delivery was clear, convincing, and solemn, his evidence was carefully prepared, and his demeanour courteous and imperturbable. The biographical sketch by Jehu Junior which accompanies the Vanity Fair cartoon in 1899 facetiously suggests that he "was a very skilful hand at eluding a question." He figured in a number of sensational trials, such as the case of Dr. George Henry Lamson (1882) who, knowing that there was no chemical test for aconitine, had administered this drug to his brother-in-law. Stevenson, however, succeeded in proving the presence of the alkaloid in the dead body.

Purely scientific research did not particularly appeal to him, and, on the whole, he found himself too busy for it. Some of his "countriness" clung to him until the end; his bodily movements were somewhat ungainly in their activity, and he possessed a "rather clumsy aptness for breaking test-tubes." A big man with a large beard which early turned grey, prominent eyebrows, and a hearty laugh, he remains a vivid personality to those who knew him.

HEARING-AIDS

Messrs. John Bell and Croyden (Wigmore-street, London, W.1) have submitted to us particulars of their Belclere series of valve-amplification hearing-aids. This comprises three models. Type S is the most powerful; Type L, less powerful, is very small and light, measuring approximately 5½ by 4 by 3¼ in. and weighing 1½ lb.; in Type W, the microphone and amplifier are contained in a small case designed to be worn in a vest pocket or under a lady's dress while the battery-case may be carried in a hip pocket. In all the models three stages of valve amplification are employed, together with a piezo-electric crystal microphone giving a very quiet background. The high-tension battery is said to last usually about three months, while the 3-volt low-tension battery gives about twenty hours of intermittent use, and is a standard Ever-Ready pattern costing sevenpence. A jelly-acid accumulator is supplied, if preferred, as an alternative. The frequency response can be corrected to suit each particular type of deafness, and this should be done in every case. The volume control is incorporated in the switch, and automatic volume control to suppress sudden loud sounds is also provided. The instruments are well designed and neatly finished; their prices are respectively 25, 20, and 18 guineas for Types S, L, and W, and they can be supplied for one week's trial before purchase.

A MODIFIED "SHIPWAY"



THE illustration shows a reconstruction of the well-known Shipway apparatus which has been designed by Dr. W. B. Primrose of Glasgow. A single rotating valve of simple pattern replaces the various rubber tube connections and non-return valves at present in use, and obviates the risk of wrong attachment. The valve, at the same time, gives any proportion of ether and/or chloroform with air or oxygen. Another position of the valve allows both bottles to be filled, the use of corks (of doubtful fit) being dispensed with. The supply and delivery tubes—the only tubes on the apparatus—are of thin flexible copper, and through their walls the vapours are heated to theatre temperature on their passage to the patient. The usual vacuum flask thus becomes unnecessary.

This compact and safe unit, with its accessories, is carried in an attaché case. The manufacturers are Anæsthetors Ltd., 163, Hope-street, Glasgow, C.2.

A.R.P. IN FACTORIES

TWO Home Office representatives attended by invitation a meeting of the Association of Industrial Medical Officers held in London on April 22nd.

Dr. N. W. Hammer, medical officer to the A.R.P. Department, said that within the scheme of the local authority factories should prepare plans to deal with their own special conditions. First-aid parties in a factory should consist of three men each, on the basis of two such parties for 250 employees, with an extra party for each additional 250 or part thereof. First-aid parties should work with rescue parties ready to give essential first-aid before sending the case to the first-aid post or hospital. Members should be trained to relieve suffering and to save life if the need arose by arresting urgent hæmorrhage or treating asphyxia from electrocution. A factory of any size should, he thought, make provision for the reception and treatment of those injured in an air-raid, as a preliminary to being sent home or transferred to hospital. The factory should also provide for the cleansing of the uninjured but contaminated. It might sometimes be well to have a medical officer at the first-aid post to do *triage* and give interim treatment—e.g., anti-shock, including transfusions, before removal to hospital. In small factories first-aid might be given in one or other of the shelters provided for protection. Casualty service personnel must not overlook the need of first-aid training for surgical conditions, including thermal burns.

Mr. H. A. Strutt, a principal under-secretary of the Home Office, spoke on the need for coöperation between the factory and the local authority. It was hoped, he said, to work out model schemes for various types of factory, so that the management might turn at once for assistance to a detailed scheme worked out for premises not unlike their own.

BAD TASTE

AMONG 1000 patients at the Vanderbilt Psychiatric Clinic, H. H. Hart found 20, all females, who complained of a bad taste in the mouth (*Arch. Neurol. Psychiat., Chicago*, April, 1938, p. 771). Of these, 9 had some form of pelvic disorder and all suffered from sexual maladjustment. On the other hand, in only 1 of the 20 could dental, oral, or nasal infection be excluded. Of another group of 44 women, attending the gynæcological clinic, two-thirds (29) complained of bad taste in the mouth. This symptom was also present in 54 of 100 patients known to have dental infection. Harper concludes that many women, particularly when suffering from dental, nasal, or pelvic disorder, may complain of a bad taste in the mouth when their sex life is frustrated. From so small a series of cases it is surely rash to draw any such conclusion. Without involving a psycho-analytical interpretation, it would be safer to infer that the state of subnormal health which must accompany dental, nasal, or pelvic disorder, may itself be the cause both of cacogeusia and frigidity.

THE INTERCEPTOR

THE chief use of this instrument is to deposit a plug of soft paraffin accurately over the os uteri where it will bar the passage of sperms from the vagina. Such a plug, it is claimed, must remain in position until removed by syringing, and it will not melt at body temperature. The Interceptor is a form of syringe ending in a detachable perforated nozzle through which the paraffin is delivered. An adjustable stop-flange ensures that the nozzle is inserted to the same depth on each occasion, and it is suggested that this should in the first place be adjusted by a doctor, the object being to ensure that the contraceptive plug is ejected at exactly the right place. Once fitted in this way the Interceptor can be used without further expert assistance. By a system of locking between inner cylinder, outer cylinder, and plunger, it becomes a syringe available for flushing or suction. It can be sterilised by boiling and in its present form is a well-finished piece of mechanism supplied in metal and leather cases. The maker, Mr. A. F. Shirreff (72, St. George's-road, London, S.W.1), has secured a patent.

Appointments

FISHER, R. E. W., M.B. Belf., Assistant Medical Officer for Air Raid Precautions for Holborn.

MACIVER, I. N., M.B. Durh., Whole-time Registrar to the Orthopædic Department of the Royal Victoria Infirmary, Newcastle-upon-Tyne.

MACKINTOSH, JEAN M., M.D. Glasg., D.P.H., Regional Medical Officer for Maternity and Child Welfare for Aberdeen.

MCKAY, MARY L., M.B. Glasg., Assistant Welfare Medical Officer for Co. Durham.

MILNER, A. N. P., M.B. N.U.I., Hon. Physician to the London Skin Hospital.

PECK, J. P. SAVILLE, M.B. Camb., Hon. Anæsthetist to the Ear, Nose, and Throat Department of the Kent and Canterbury Hospital.

RUSSEL, J. M., M.B. Edin., B.Hy., D.P.H., Temporary Assistant Medical Officer for Co. Durham.

RYAN, J. E., M.B. Melb., F.R.C.S. Edin., a Consulting Gynæcologist to the Charterhouse Rheumatism Clinic.

SCOTT, MARY, M.B., Hon. Anæsthetist to the Kent and Canterbury Hospital.

TIMONEY, JOSEPH, M.B. N.U.I., Assistant Medical Officer at the Wakefield Mental Hospital.

WAY, STANLEY, M.R.C.S. Eng., Whole-time Junior Gynæcological and Obstetrical Registrar at the Royal Victoria Infirmary, Newcastle-upon-Tyne.

London County Council Hospital Staff.—The following promotions in the mental services are announced. A.M.O. = Assistant Medical Officer:—

BLAIR, D. A. S., M.B. Camb., D.P.M., a Second A.M.O., Cane Hill Hospital;

BUTLER, E. N., B.M. Oxon., D.P.M., a Second A.M.O., Caterham Hospital;

KIRMAN, B. H., M.D. Lond., D.P.M., a Second A.M.O., Darenth Park;

STOKES, A. B., B.M. Oxon., M.R.C.P. Lond., D.P.M., a Second A.M.O., Maudsley Hospital;

THORLEY, A. S., M.B. Lond., D.P.M., a Second A.M.O., Friern Hospital; and

WHELEN, MAEVE, M.B. Lond., D.P.M., a Second A.M.O., Tooting Bec Hospital.

County Council of Middlesex.—The following appointments are announced:—

ASHER, R. A. J., M.B. Lond., Assistant Medical Officer, West Middlesex County Hospital;

CHIVERS, ELVA, M.B. Cape Town, D.A., Assistant Medical Officer (Anæsthetist), West Middlesex County Hospital;

TITCOMBE, I. M., B.M. Oxon., Obstetrician (Grade II), West Middlesex County Hospital;

JENNINGS, G. H., M.B. Camb., M.R.C.P. Lond., Physician (Grade I), Redhill County Hospital;

ROSSER, E. AP I., M.B. Lond., M.C.O.G., Obstetrician (Grade I), Redhill County Hospital;

SNAITH, L., M.S. Durh., F.R.C.S. Eng., M.C.O.G., Obstetrician (Grade II), North Middlesex County Hospital; and

HOUGHTON, L. E., M.D. Camb., Physician (Grade I), County Sanatorium, Harefield.

Hospital for Sick Children, Great Ormond-street, W.C.—The following appointments are announced:—

BONHAM-CARTER, R. E., M.B. Camb., M.R.C.P. Lond., Resident Assistant Physician;

FIELD, CONSTANCE, M.D. Lond., Resident Medical Assistant and Clinical Pathologist;

ILLINGWORTH, R. S., M.D. Leeds, D.P.H., Resident Medical Assistant and Clinical Pathologist;

GAIRDNER, DOUGLAS, M.B. Camb., Out-patient Medical Officer; and

LANDAU, MARJORIE, M.B. Lond., House Surgeon.

Colonial Medical Service.—The following appointments and promotions are announced:—

BEATTIE, D. A., M.B. Lond., F.R.C.S. Eng., Medical Officer, Malaya;

FORBES-WINSLOW, V. F., M.R.C.S., D.P.H., Medical Officer, West Africa;

HOLLINS, C., B.M. Oxon., Medical Officer, West Africa;

THOMSON, E. S. O., M.B. Edin., Woman Medical Officer, Malaya;

DEALE, J. E., M.B. Dubl., F.R.C.S. Irel., Senior Medical Officer, Gibraltar;

GILLESPIE, A. M., M.B., F.R.C.P. Edin., D.T.M., Senior Specialist, Gold Coast;

LAWRIE, E. S., M.B. Glasg., Surgeon, Grade B, Malayan Medical Service;

MACLENNAN, N. M., M.D. Aberd., D.P.H., D.T.M. and H., Director of Medical Services, British Guiana: and

WALKINGSHAW, R., M.B. Glasg., D.T.M. and H., Surgeon, Grade B, Malayan Medical Service.

Certifying Surgeons under the Factory and Workshop Acts: Dr. D. R. ASHTON (Yaxley District, Huntingdon); Dr. J. S. MACGILL (Denton District, Lancaster); Dr. A. L. E. F. COLEMAN (Anstey District, Leicester); Dr. R. D. SCOTT (Andover District, Southampton).